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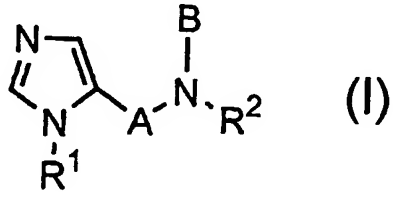
(54) Title: THIOUREA AND ISOTHIOUREA DERIVATIVES FOR INHIBITING RAS-TRANSFORMED CELL GROWTH



(I)

(57) Abstract: The present invention relates to thiourea and isothiourea derivatives of formula (I) or pharmaceutically acceptable salt thereof which possess excellent activity for inhibiting ras-transformed cell growth wherein, A, B, R^1, R^2, R^3, R^4, R^5 and R^6 have the same meaning as defined in the specification.

THIOUREA AND ISOTHIOUREA DERIVATIVES FOR INHIBITING RAS-TRANSFORMED CELL GROWTH

Field of the Invention

The present invention relates to novel thiourea and isothiourea derivatives or pharmaceutically acceptable salts thereof which possess excellent activity for inhibiting ras-transformed cell growth, to processes for the preparation thereof, and to a pharmaceutical composition for the inhibition of ras-transformed cell growth comprising the same as an active ingredient.

Background of the Invention

A ras protein is farnesylated or geranylgeranylated by farnesyltransferases [farnesyl protein transferase (hereinafter referred to as "FPTase") or geranylgeranyl protein transferase (hereinafter referred to as "GGPTase"), respectively], and then, translocated into an intracelluar membrane, in which the ras protein is activated by GTP or inactivated by GDP. The activated, GTP-bound ras protein triggers the stepwise transmission of the outside signal into nucleus, which, in turn, activates translational factors of cells such as myc, jun and fos, thereby leading to cell growth or nucleus division. (see M. Barbacid, Annu. Rev. Biochem., 56, 779, 1987, P J. Casey et al., Natl. Acad. Sci. U.S.A. 86, 8323, 1989).

When a transformed ras protein variant such as H-Ras, N-Ras, K-RasA and K-RasB derived from mutated ras genes is activated, it remains activated, and causes cell tumorization as the result of unregulated cell growth. The mutated ras genes are found in various cancer cases, e.g., colon cancer (about 50%), pancreas cancer (about 90%), lung cancer (about 50%), and thyroid gland cancer (about 30%) (see S. Rodenhuis, Semin. Cancer Biol. 3, 241, 1992).

A number of researches have attempted to develop inhibitors of ras protein variants, focusing mostly on FPTase inhibitors which inhibit the translocation of ras proteins into an intracellular membrane. For example, Cys-Val-Phe-Met, a sequence similar to the C-terminal sequence of ras protein(Cys-A1-A2-Met), has been reported (see J. L. Goldstein et al., J. Biol. Chem., 266, 15575, 1991; A. M. Garcia et al., J. Biol. Chem., 268, 18415, 1993; S. L. Graham et al., J. Med. Chem., 37, 725, 1994).

Further, various derivatives mimicking Cys-Ile-Phe-Met as a prototype inhibitor have been developed. For example, aromatic alkylamine derivatives wherein the Phe-Met moiety is displaced by an aromatic alkylamine(see S. J. Desolms et al., J. Med. Chem., 38, 3967, 1995) and carbonylamide derivatives wherein aminomethylnaphthalene is combined with cysteine and trans-3(S)-ethylproline(see WO9606609, 1996) have been reported to have FPTase inhibitory activity. And pseudopeptide derivatives containing substituted imidazolethyl group in place of cysteine have been reported to have FPTase inhibitory activity (see J. H. Hunt et al., J. Med. chem., 39, 353, 1996; WO9610035, 1996; WO9610034, 1996; WO9609836, 1996). Further, WO9639173 discloses that compounds containing p-cyanobenzyl-imidazolacetate in place of cysteine and N-naphthylmethyl in place of phenylalanine, respectively, in the structure of Cys-Ile-Phe-Met, have FPTase inhibitory activity.

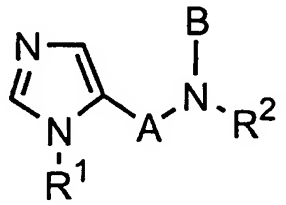
However, it has been pointed out that the above FPTase inhibitors can not effectively inhibit the geranylgeranylation of the K-ras protein, i.e., the most frequently found ras-protein variant in human cancer. Therefore, FPTase inhibitors fail to inhibit the prenylation of the K-ras protein in cells (see G. L. James et al., J. Biol. Chem. 270, 6221, 1995).

The present inventors have endeavored to develop ras-transformed cell growth inhibitors which is capable of blocking the prenylation of the K-ras protein more effectively; and have discovered that novel thiourea or isothiourea derivatives exhibit excellent activity for inhibiting K-ras prenylation as well as

ras-transformed cell (per se) growth.

Summary of the Invention

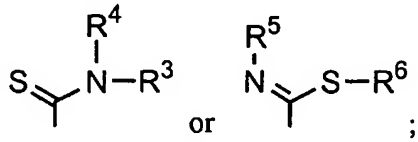
Accordingly, it is a primary object of the present invention to provide a compound of formula (I) or a pharmaceutically acceptable salt thereof:



(I)

wherein,

A is $-(CH_2)_n-$ or $-(CH_2)_n-C(=O)-$, n being an integer from 1 to 4;

B is  or ;

R^1 is C_{1-4} alkyl, or benzyl optionally having one or more ring substituents selected from the group consisting of cyano, nitro and methylenedioxy;

R^2 is C_{1-5} alkyl, C_{2-5} alkenyl; C_{5-7} cycloalkylmethyl; C_{1-3} alkylphenyl; a ring containing group selected from the group consisting of benzyl, α -methylbenzyl, naphthylmethyl, pyrrolymethyl, pyridylmethyl, indolylmethyl, and quinolylmethyl, each optionally having one or more ring substituents selected from the group consisting of C_{1-3} alkyl, halogen, C_{1-3} alkoxy, and trifluoromethyl;

R^3 is C_{1-10} alkyl; C_{2-5} alkenyl; C_{3-8} cycloalkyl; adamantyl; C_{1-5}-alkoxy-C_{1-5}-alkyl; mono- or di- C_{1-5}-alkylamino-C_{1-5}-alkyl; C_{1-5} alkoxylcarbonyl; phenyl-C_{1-5}-alkyl; tetrahydrofuranyl-C_{1-5}-alkyl; a nitrogen-containing heterocycle group selected from the group consisting of pyridyl, pyrimidyl, piperidyl, piperazyl, morphorinyl, and

morphorinyl-C_{1-5}-alkyl, each heterocyclo being optionally substituted with C_{1-3} alkyl or C_{1-3} alkoxy; an aromatic ring containing group selected from the group consisting of phenyl, naphthyl, and benzoyl, each optionally having one or more ring substituents selected from the group consisting of C_{1-5} alkyl, C_{1-5} alkoxy, C_{1-5} alkylthio, mono- or di-C_{1-5}-alkylamino, trifluoromethyl, benzyloxy, hydroxy, halogen, cyano, nitro, C_{1-5} alkoxycarbonyl, acetyl, and phenyl;

R^4 is hydrogen or C_{1-4} alkyl;

R^5 is phenyl optionally having one or more substituents selected from the group consisting of halogen, C_{1-5} alkyl, C_{1-5} alkoxy, and trifluoromethyl; benzyl; or pyridyl optionally substituted with hydroxy or methoxy; and

R^6 is C_{1-10} alkyl, C_{2-5} alkenyl, or benzyl with one or more optional ring substituents selected from the group consisting of C_{1-5} alkoxy, cyano and nitro.

It is another object of the present invention to provide processes for preparing the compound of formula (I).

It is a further object of the present invention to provide a pharmaceutical composition for the inhibition of ras-transformed cell growth comprising a therapeutically effective amount of a compound or salt of formula(I) as an active ingredient together with a pharmaceutically acceptable carrier.

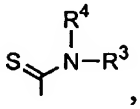
Detailed Description of the Invention

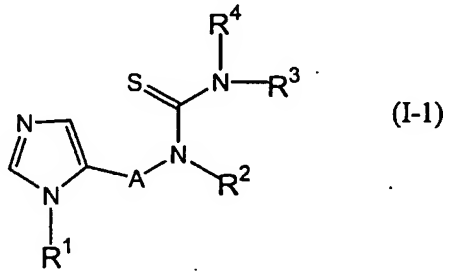
The pharmaceutically acceptable salt of the thiourea or isothiourea derivative of the present invention is a non-toxic salt generated from an inorganic acid, e.g., hydrochloric acid, hydrobromic acid, sulfuric acid, sulfamic acid, phosphoric acid and nitric acid, or an organic acid e.g., acetic acid, propionic acid, succinic acid, glycolic acid, stearic acid, citric acid, maleic acid, malonic acid, methanesulfonic acid, tartaric acid, malic acid,

hydroxymalic acid, phenylacetic acid, glutamic acid, benzoic acid, salicylic acid, 2-acetoxybenzoic acid, fumaric acid, toluenesulfonic acid, oxalic acid or trifluoroacetic acid.

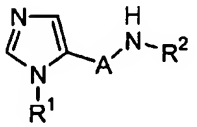
Among the compound of formula (I) of the present invention, the preferred are those wherein R^1 is benzyl optionally substituted with cyano, nitro or methylenedioxy; R^2 is benzyl optionally substituted with halogen, C_{1-5} alkyl or trifluoromethyl; R^3 is C_{1-3} alkoxypyridyl; or phenyl optionally substituted with halogen, C_{1-5} alkyl, C_{1-5} alkoxy, trifluoromethyl, hydroxy, C_{1-5} alkylthio, or C_{1-5} alkoxycarbonyl; and R^6 is C_{1-10} alkyl.

The present invention also provides processes for preparing thiourea and isothiourea derivatives of formula(I).

For example, a thiourea compound of formula(I-1), corresponding to the compound of formula(I) wherein B is  , may be prepared by the process which comprises reacting a compound of formula (XXXII) with a compound of formula (XXXIII) or (XXXIV):



(I-1)

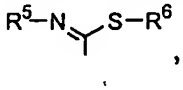


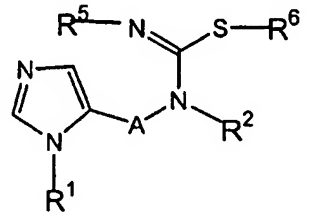
(XXXII)

(R^3)-N=C=S (XXXIII)

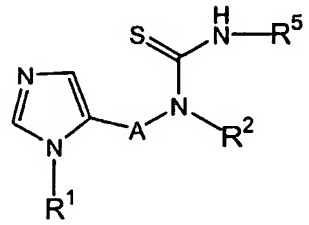
$(R^3)(R^4)$-N-C(=S)-Cl (XXXIV)

wherein A, R^1, R^2, R^3 and R^4 have the same meaning as defined above.

Further, an isothiourea compound of formula(I-2), corresponding to the compound of formula(I) wherein B is  , may be prepared by the process which comprises reacting a compound of formula (If) with a compound of formula (XXXV):



(I-2)



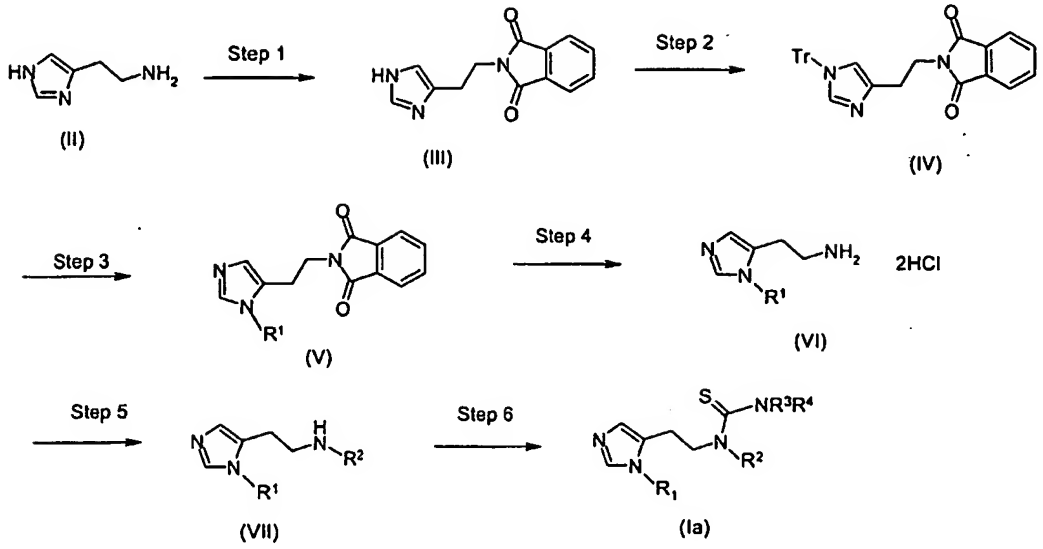
(If)

R^6-X (XXXV)

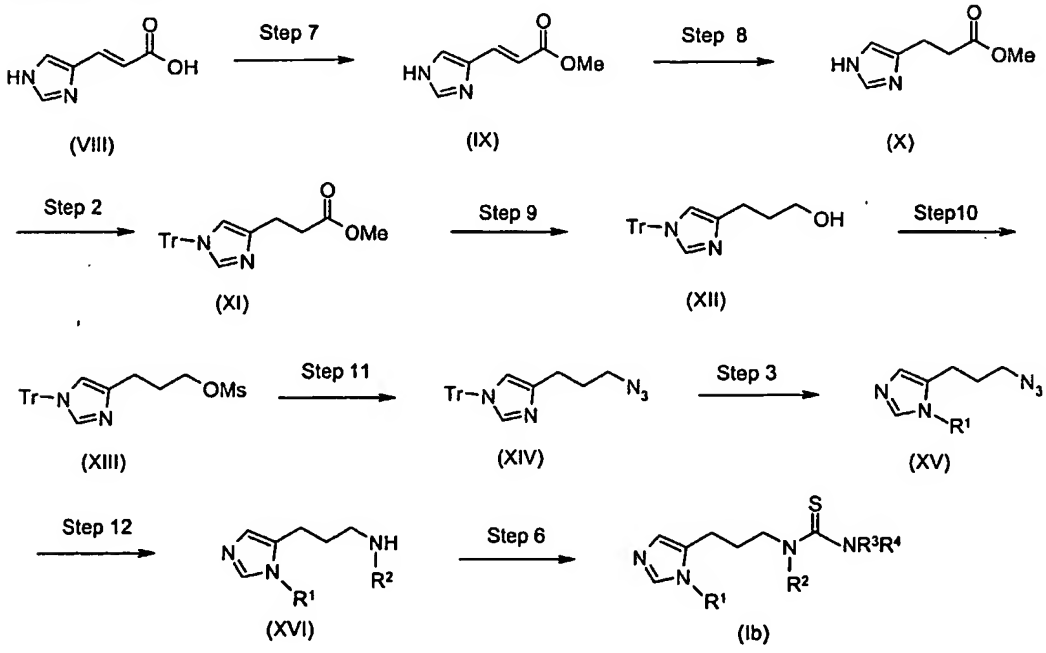
wherein R^1, R^2, R^5, R^6 and A have the same meaning as defined above.

The processes for preparing the compound of formula(I) may be conducted in accordance with Reaction Schemes 1 to 6 as described below :

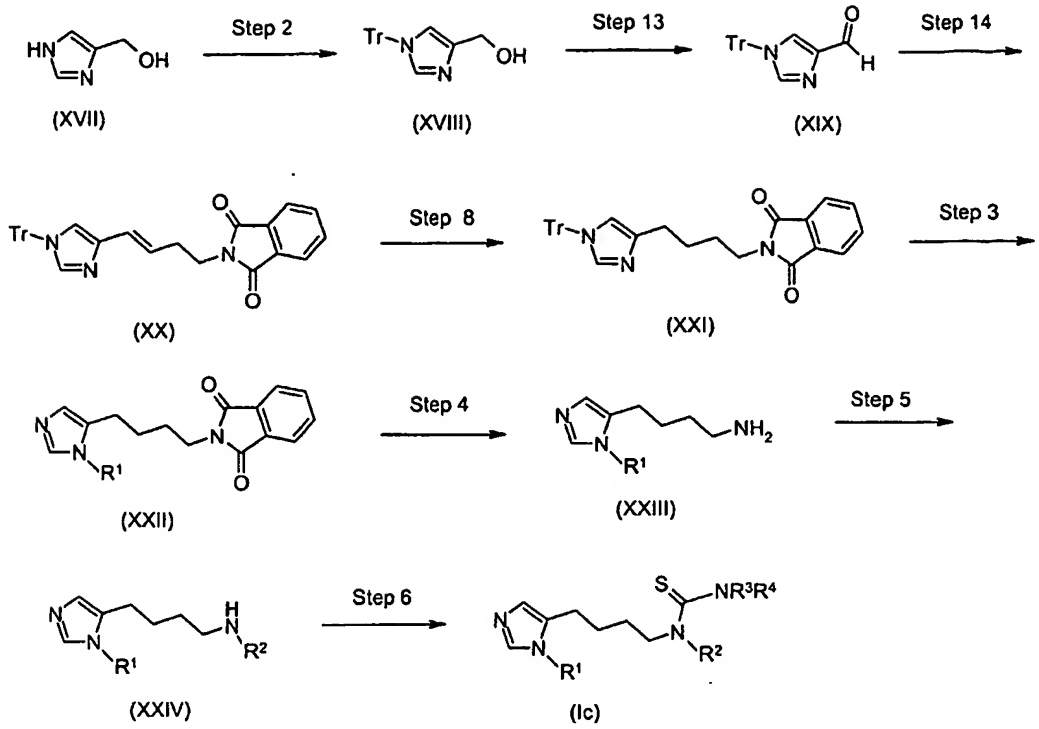
Reaction Scheme 1



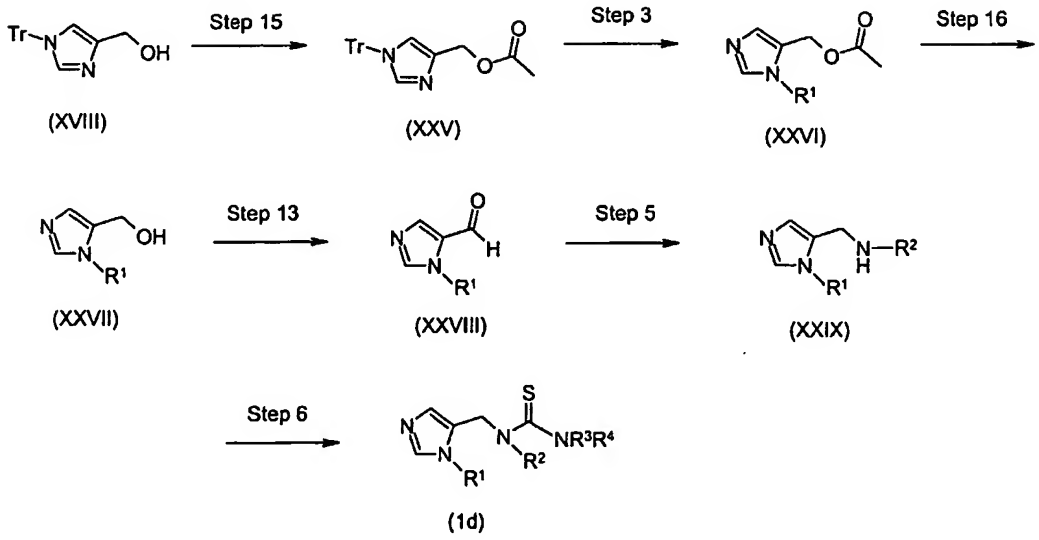
Reaction Scheme 2



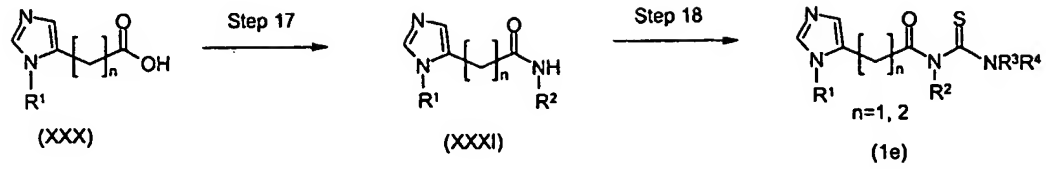
Reaction Scheme 3



Reaction Scheme 4

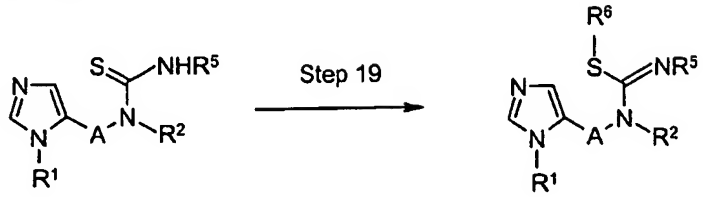


Reaction Scheme 5



(XXX) (XXXI) (1e)

Reaction Scheme 6



(If) (Ig)

In the above Reaction Schemes, R^1, R^2, R^3, R^4, R^5, R^6, and A have the same meanings as defined previously, and Tr is triphenylmethyl.

The processes summarized in the above Reaction Schemes may be conducted in a conventional manner and typical procedures thereof are described below.

Step 1. Amine protection

The compound of formula(II) is reacted with N-ethoxycarbonyl phthalimide to give the compound of formula(III) to protect the primary amine group.

Step 2. Imidazole protection

The compounds of formula(III), (X) and (XVII) are each dissolved in an appropriate organic solvent and then reacted with triphenylmethyl chloride to give the compounds of formula (IV), (XI) and (XVIII), respectively.

Step 3. Addition

The compound of formula(IV), (XIV), (XXI) and (XXV) are each dissolved in an appropriate organic solvent and then reacted with R^1-X (X is halogen) to give compounds of formula(V), (XV), (XXII) and (XXVI) , respectively.

The organic solvent may be selected from dichloromethane, dimethylformamide, acetonitrile, methanol, ethyl acetate or a mixture thereof. To facilitate the reaction, the reaction mixture can be heated.

Step 4. Deprotection

Compounds of formula(V) and (XXII) are each reacted with hydrazine to remove the amino-protecting group giving compounds of formula(VI) and (XXIII) , respectively.

Step 5. Reductive alkylation

Compounds of formula(VI) and (XXIII) are each reacted with an aldehyde capable of providing R^2 moiety in the presence of sodium cyanoborohydride or other conventional reducing agent, to give compounds of formula(VII) and (XXIV), respectively. This reaction can be facilitated by the addition of potassium acetate or acetic acid and 3Å molecular sieve. The compound of formula(XXVIII) may be reacted with an amine of R^2-NH_2 under the same condition as described in the above to give the compound of formula(XXIX).

Step 6. Addition

Compounds of formula(VII), (XVI), (XXIV) and (XXIX) are each reacted with (R^3)-N=C=S or (R^3)(R^4)-N-C(=S)-Cl in dimethylformamide, dichloromethane or acetonitrile to give compounds of formula(Ia), (Ib), (Ic) and (Id) , respectively.

Step 7. Esterification

The compound of formula (VIII) is reacted with an alcohol under an acidic condition to give the compound of formula(IX).

Step 8. Hydrogenation

The compounds of formula(IX) and (XX) are each reacted with hydrogen in the presence of a catalyst(e.g.: palladium and rhodium) to give the compounds of formula(X) and (XXI), respectively. The preferred solvent for this reaction is dimethylformamide, ethanol or ethyl acetate.

Step 9. Reduction

The compound of formula(XI) is reacted with lithium aluminium hydride in tetrahydrofuran or diethyl ether, to give the compound of formula(XII).

Steps 10, 11, and 15. Substitution

The compound of formula(XII) is reacted with methanesulfonyl chloride in the presence of an organic bases, to give the compound of formula(XIII).

The compound of formula(XIII) is reacted with sodium azide in dimethylformamide or hexamethylphosphoramide to give the compound of formula(XIV).

The compound of formula(XVIII) is reacted with acetic anhydride or acetyl halide in the presence of an organic base to give the compound of formula(XXV).

Step 12. Reductive alkylation

A compound of formula(XV) is reacted with an aldehyde capable of providing R^2 moiety in the presence of triphenylphosphine and sodium borohydride or other conventional reducing agent to give the compound of

formula(XVI).

Step 13. Oxidation

The compound of formula(XVIII) or a compound of formula(XXVII) is reacted with pyridine-sulfur trioxide complex or other conventional oxidizing agent to give the compound of formula(XIX) or a compound of formula(XXVIII), respectively.

Step 14. Olefination

The compound of formula(XIX) is reacted with a ylide prepared from the reaction of 3-halophthalimide with triphenylphosphine in the presence of a base such as potassium t-butoxide, to give the compound of formula(XX).

Step 16. Hydrolysis

A compound of formula(XXVI) is hydrolyzed in water, or in a mixture of tetrahydrofuran and water in the presence of an alkali or acid condition to give a compound of formula(XXVII).

Step 17. Amide formation

A compound of formula(XXX) is reacted with an amine R^2-NH_2 in the presence of an appropriate coupling agent to give a compound of formula(XXXI). The coupling agent may be hydroxybenzotriazole or dialkylcarbodiimidate. A suitable solvent may be dimethylformamide, dichloromethane or a mixture thereof.

Step 18. Addition

A compound of formula(XXXI) is reacted with with (R^3)-N=C=S or (R^3)(R^4)-N-C(=S)-Cl in the presence of an appropriate base such as sodium hydride and potassium carbonate to give a compounds of formula(Ie). A suitable solvents for this reaction is dimethylformamide, dimethylsulfoxide or

hexamethylphosphoamide.

Step 19. Alkylation

A compound of formula(If) may be reacted with R^6-X (X is halogen) in dichloromethane, methanol, ethanol, acetonitrile, acetone or dimethylformamide, optionally in the presence of a base such as sodium hydroxide, potassium carbonate or triethylamine, to give a compound of formula(Ig).

The non-toxic pharmaceutically acceptable salts of the compound(I) may be prepared according to conventional methods known per se in the art, by reacting the compound in an appropriate solvent with a stoichiometric or excess amount of an inorganic or organic acid.

The present invention also includes within its scope a pharmaceutical composition for the inhibition of ras-transformed cell growth comprising a therapeutically effective amount of the novel compounds of formula(I), as defined above, or a pharmaceutically acceptable salt thereof as an active ingredient together with a pharmaceutically acceptable carrier.

The composition of the present invention may include additives such as lactose or corn starch, lubricant such as magnesium stearate, or conventional emulsifier, suspending agent, stabilizer, isotonic agent. If necessary, sweetener and/or flavoring agent may be added.

The composition of the present invention may be administered orally or parenterally, including intravenous, intraperitoneal, subcutaneous, rectal and topical routes of administration. Therefore, the composition of the present invention may be formulated into various forms such as tablets, capsules, aqueous solutions or suspensions. In case of tablets for oral use, carriers such as lactose, corn starch, and lubricating agents, e.g. magnesium stearate, are commonly added. For oral administration in capsule form, lactose and/or dried corn starch can be used as a diluent. When an aqueous suspension are required

for oral use, the active ingredient may be combined with emulsifying and/or suspending agents. If desired, certain sweeteners and/or flavoring agents may be added. For intramuscular, intraperitoneal, subcutaneous and intravenous use, sterile solutions of the active ingredient are usually prepared, and the pH of the solutions should be suitably adjusted and buffered. For intravenous use, the total concentration of solutes should be controlled in order to render the preparation isotonic. The composition of the present invention may be in the form of aqueous solution containing pharmaceutically acceptable carriers, e.g., saline, at a pH level of 7.4. The solutions may be introduced into a patient's intramuscular blood-stream by local bolus injection.

The compounds of the present invention may be administered in an effective amount ranging from about 0.1mg/kg to about 20mg/kg, preferably from about 0.5mg/kg to about 10mg/kg, per day into a subject patient suffered from various cancers, e.g., colorectal carcinoma, exocrine pancreatic carcinoma, and myeloid leukemias. Of course, the dosage may be changed according to patient's age, weight, susceptibility, or symptom.

The following Examples are given for the purpose of illustration only, and are not intended to limit the scope of the invention.

Preparation Example 1

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-trifluoromethyl-benzylamine

<Step 1>

N-[2-(1H-Imidazol-4-yl)]ethyl phthalimide

To a solution of histamine 2HCl(21.5g, 0.12mol) in distilled water(300ml) was added sodium carbonate(37.1g 0.35mol). N-ethoxycarbonylphthalimide(25.6g, 0.12mol) was added dropwise to above solution and the reaction mixture was stirred for 24hr at room temperature. The resulting solid was filtered, washed with water(50ml) and n-hexane(50ml). The title compound(20g) as a white solid to give after dried under in vacuo.

^{1}H-NMR(DMSO-d_6 + TFA-d_1) δ 8.95(s, 1H), 7.78(m, 4H), 7.43(s, 1H), 3.85(t, 2H), 2.98(t, 2H),

<Step 2>

N-[2-(1-Triphenylmethyl-imidazol-4-yl)]ethyl phthalimide

To a solution of N-[2-(1H-imidazol-4-yl)]ethyl phthalimide(20.0g, 82.9mmol) and triethylamine(23.0ml, 166mmol) in co-solvent of DMF(50ml) and dichloromethane(200ml) was added dropwise triphenylmethyl chloride(27.7g, 99.5mmol) under ice-water bath. After the stirring for 24hr at room temperature, dichloromethane(200ml) was added to the reaction mixture. The mixture was washed with water and brine. The organic layer was dried over anhydrous magnesium sulfate, concentrated *in vacuo* to give an oily material. The residue was recrystallized from n-hexane to provide a white solid of the title compound(40g).

^{1}H-NMR(DMSO-d_6) δ 7.8(m, 4H), 7.3(m, 9H), 7.2(s, 1H), 7.0(m, 6H), 6.6(s,

1H), 3.8(t, 2H), 2.8(t, 2H)

<Step 3>

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl phthalimide HBr

A suspension of N-[2-(1-triphenylmethyl-imidazol-4-yl)]ethyl phthalimide(40g, 82.7mmol) and 4-cyanobenzyl bromide(19.7g, 91.2mmol) in acetonitile(250ml) were stirred for 24hr at 50-60°C. The reaction mixture was concentrated *in vacuo* to give an oily material. After the addition of methanol(200ml), the reaction mixture was refluxed for 3hr. The solution was concentrated *in vacuo* to the volume of 50 ml. Ethyl acetate(200ml) was added, and the solution was stirred for 1hr under ice-water bath. The collected solid by filtration was dried *in vacuo* to give a white solid of the title compound(30.9g). ^{1}H-NMR(DMSO-d_6) δ 9.32(s, 1H) 7.8(m, 6H), 7.65(s, 1H), 7.5(d, 2H), 5.65(s, 2H), 3.75(t, 2H), 2.90(t, 2H),

<Step 4>

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl phthalimide HBr(30g, 65.6mmol) in methanol(100ml) was added hydrazine hydrate(6.4ml, 131.2mmol). The reaction mixture was refluxed for 1.5hr and then HCl gas was passed the reaction mixture under ice-water bath. The resulting insoluble material was filtered off. The resulting filtrate was concentrated *in vacuo* and the solid residue was washed with ethyl acetate(50ml), dried in vacuo to give a pale yellow solid of the title compound(25g).

<Step 5>

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-trifluoromethylbenzylami

ne

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(8.5g, 28.4mmol) and 2-(trifluoromethyl)benzaldehyde(3.7ml, 28.4mmol) in methanol(100ml) were added molecular sieve(3Å, 30g), and acetic acid(0.5ml). The reaction mixture was stirred for 30 minute at room temperature, and sodium cyanoborohydride(2.7g, 42.6mmol) was added dropwise under ice-water bath. The reaction mixture was stirred for 2hr at room temperature. After the removal of insoluble material by filtration, the filtrate was concentrated *in vacuo* to give a pale yellow liquid. The residue was dissolved in ethyl acetate(200ml), washed with water and saturated $NaHCO_3$ solution. The organic layer was dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give a liquid of the title compound(4.0g).

^{1}H-NMR($CDCl_3$) δ 7.51-7.65(m, 6H), 7.35-7.39(m, 1H), 7.09(d, 2H) 6.92(s, 1H), 5.17(s, 2H), 3.89(s, 2H), 2.82(t, 2H), 2.60(t, 2H)

Preparation Example 2

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2,3-dichlorobenzyl-amine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(900mg, 3.01mmol) prepared from <Step 4> of Preparation Example 1 and 2,3-dichlorobenzaldehyde(526mg, 3.01mmol) in methanol(20ml) were added molecular sieve(3Å, 3.0g), and acetic acid(0.5ml). The reaction mixture was stirred for 30 minute at room temperature, and sodium cyanoborohydride(378mg, 6.02mmol) was added dropwise under ice-water bath. The reaction mixture was stirred for 4hr at room temperature. After the

removal of insoluble material by filtration, the filtrate was concentrated *in vacuo* to give a pale yellow liquid. The residue was dissolved in ethyl acetate(200ml), washed with water and saturated $NaHCO_3$ solution. The organic layer was dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give a liquid of the title compound(334mg, 49%).

R_f=0.3(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.49(s, 1H), 7.35-7.40(m, 1H), 7.20-7.26(m, 2H), 7.07(d, 2H), 6.91(s, 1H), 5.15(s, 2H), 3.84(s, 2H), 2.81(t, 2H), 2.59(t, 2H)

Preparation Example 3

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-chlorobenzylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(2.05g, 6.12mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(769mg, 12.2mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 2-chlorobenzaldehyde(1.03g, 7.33mmol), to give the title compound(462mg, 20%).

R_f=0.2(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.59(d, 2H), 7.50(s, 1H), 7.32-7.37(m, 1H), 7.18-7.30(m, 3H), 7.07(d, 2H), 6.90(s, 1H), 5.15(s, 2H), 3.82(s, 2H), 2.78(t, 2H), 2.59(t, 2H)

Preparation Example 4

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-3-chlorobenzylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(2.05g, 6.12mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(769mg, 12.2mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 3-chlorobenzaldehyde(1.03g, 7.33mmol), to give the title compound(580mg, 27%).

R_f=0.2(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.61(d, 2H), 7.50(s, 1H), 7.22-7.27(m, 3H), 7.05-7.13(m, 3H), 6.91(s, 1H), 5.15(s, 2H), 3.71(s, 2H), 2.77(t, 2H), 2.58(t, 2H)

Preparation Example 5

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-fluorobenzylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(1.88g, 5.61mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(769mg, 12.2mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 2-fluorobenzaldehyde(694mg, 5.61mmol), to give the title compound(868mg, 46%).

R_f=0.2(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.61(d, 2H), 7.49(s, 1H), 7.13-7.28(m, 2H), 6.98-7.17(m, 4H), 6.89(s, 1H), 5.15(s, 2H), 3.78(s, 2H), 2.78(t, 2H), 2.59(t, 2H)

Preparation Example 6

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-3-fluorobenzylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(2.05g, 6.12mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(769mg, 12.2mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 3-fluorobenzaldehyde(0.78ml, 6.12mmol), to give the title compound(419mg, 21%).

R_f=0.2(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.61(d, 2H), 7.49(s, 1H), 7.24-7.27(m, 1H), 7.07(d, 2H), 6.90-7.05(m, 4H), 5.15(s, 2H), 3.72(s, 2H), 2.77(t, 2H), 2.58(t, 2H)

Preparation Example 7

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-methylbenzylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(2.05g, 6.12mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(769mg, 12.2mmol) and replacing 2-(trifluoromethyl)benzaldehyde with *o*-tolualdehyde(0.85ml, 6.12mmol), to give the title compound(222mg, 11%).

R_f=0.2(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.59(d, 2H), 7.48(s, 1H), 7.13-7.17(m, 4H), 7.07(d, 2H), 6.91(s, 1H), 5.15(s, 2H), 3.71(s, 2H), 2.84(t, 2H), 2.59(t, 2H), 2.28(s, 3H)

Preparation Example 8

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2,3-difluorobenzylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(2.05g, 6.12mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(769mg, 12.2mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 2,3-difluorobenzaldehyde(0.80ml, 6.12mmol), to give the title compound(898mg, 42%).

R_f=0.2(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.61(d, 2H), 7.49(s, 1H), 7.09(d, 2H), 7.00-7.06(m, 3H), 6.69(s, 1H), 5.16(s, 2H), 3.80(s, 2H), 2.77(t, 2H), 2.58(t, 2H)

Preparation Example 9

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2,6-difluorobenzyl-amine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(2.05g, 6.12mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(769mg, 12.2mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 2,6-difluorobenzaldehyde(0.80ml, 6.12mmol), to give the title compound(950mg, 44%).

R_f=0.2(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.59(d, 2H), 7.48(s, 1H), 7.18-7.26(m, 1H), 7.07(d, 2H), 6.82-6.90(m, 3H), 5.15(s, 2H), 3.82(s, 2H), 2.73(t, 2H), 2.57(t, 2H)

Preparation Example 10

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-4-trifluoromethyl-benzylam ine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(4.52g, 13.5mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(1.70g, 27.0mmol) and replacing 2-(trifluoromethyl)benzaldehyde with α,α,α-trifluoro-*p*-tolualdehyde(2.35g, 13.5mmol), to give the title compound(2.38g, 46%).

Preparation Example 11

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(1-methyl-1H-pyrrol-2yl)methylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(900mg, 4.0mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(300mg, 4.8mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 1-methyl-2-pyrrolecarboxaldehyde(430ul, 4.0mmol), to give the title compound(260mg, 20%).

R_f=0.25(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.62(d, 2H), 7.50(s, 1H), 7.10(d, 2H), 6.90(s, 1H), 6.60(s, 1H), 6.05(t, 1H), 5.97(s, 1H), 5.20(s, 2H), 3.70(s, 2H), 3.60(s, 3H), 2.82(t, 2H), 2.60(t, 2H)

Preparation Example 12

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(1H-indol-3-yl)-methylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(900mg, 4.0mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(300mg, 4.8mmol) and replacing 2-(trifluoromethyl)benzaldehyde with indole-3-carboxaldehyde(0.58ml, 4.0mmol), to give the title compound(330mg, 23%).

R_f=0.05(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 8.20(bs, 1H), 7.45-7.62(m, 3H), 7.40(d, 1H), 7.10-7.20(m, 2H), 7.00(t, 3H), 6.90(s, 1H), 5.10(s, 2H), 4.00(s, 2H), 2.82(t, 2H), 2.60(t, 2H)

Preparation Example 13

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(1-methyl-1H-indol-3-yl)methylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(790mg, 3.5mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(260mg, 4.2mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 1-methylindole-3-carboxaldehyde(0.56g, 3.5mmol), to give the title compound(260mg, 20%).

R_f=0.05(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.60(m, 2H), 7.50(d, 2H), 7.30(m, 2H), 7.13(m, 1H), 7.00(d, 2H), 6.92(d, 2H), 5.10(s, 2H), 4.00(s, 2H), 3.80(s, 3H), 2.85(t, 2H), 2.60(t, 2H)

Preparation Example 14

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(2-methyl-1H-indol-3-yl)methylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(1000mg, 4.5mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(340mg, 5.4mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 2-methylindole-3-carboxaldehyde(720mg, 4.5mmol), to give the title compound(570mg, 34%).

R_f=0.05(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.52(d, 2H), 7.48(s, 1H), 7.40(d, 1H), 7.30(m, 1H), 7.10(m, 2H), 7.00(d, 2H), 6.78(s, 1H), 5.02(s, 2H), 3.85(s, 2H), 2.78(t, 2H), 2.60(t, 2H), 2.35(s, 3H)

Preparation Example 15

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(5-methoxy-1H-indol-3-yl)methylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(1000mg, 4.5mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(340mg, 5.4mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 5-methoxyindole-3-carboxaldehyde(720mg, 4.5mmol), to give the title

compound(330mg, 19%).

R_f=0.05(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.60(s, 1H), 7.50(d, 2H), 7.30(d, 1H), 7.00(m, 4H), 5.10(s, 2H), 4.00(s, 2H), 3.85(s, 3H), 2.78(t, 2H), 2.60(t, 2H)

Preparation Example 16

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(6-methyl-pyridin-2-yl)methylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(790mg, 3.5mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(260mg, 4.2mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 6-methyl-2-pyridinecarboxaldehyde(420mg, 3.5mmol), to give the title compound(140mg, 12%).

R_f=0.20(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.50(s, 1H), 7.15(d, 2H), 7.05(d, 2H), 6.92(s, 1H), 5.20(s, 2H), 3.82(s, 2H), 2.85(t, 2H), 2.65(t, 2H), 2.55(s, 3H)

Preparation Example 17

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(2,6-dichloro-pyridin-3-yl)methylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(1.0g, 4.5mmol)

prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(0.34g, 5.4mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 2,6-dichloropyridine-3-carboxaldehyde(0.79g, 4.5mmol), to give the title compound(1.1g, 63%).

R_f=0.15(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.65(m, 3H), 7.52(s, 1H), 7.22(d, 1H), 7.10(d, 2H), 6.92(s, 1H), 5.20(s, 2H), 3.80(s, 2H), 2.80(t, 2H), 2.60(t, 2H)

Preparation Example 18

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(2-chloro-pyridin-3-yl)methylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(1.4g, 6.2mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(0.47g, 7.4mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 2-chloropyridine-3-carboxaldehyde(0.88g, 6.2mmol), to give the title compound(1.0g, 46%).

R_f=0.25(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 8.28(dd, 1H), 7.65(dd, 1H), 7.60(d, 2H), 7.50(s, 1H), 7.20(m, 1H), 7.05(d, 2H), 6.92(s, 1H), 5.20(s, 2H), 3.80(s, 2H), 2.80(t, 2H), 2.60(t, 2H)

Preparation Example 19

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(6-chloro-pyridin-2-yl)meth

ylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(1.2g, 5.3mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(0.4g, 6.4mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 6-chloropyridine-2-carboxaldehyde(0.75g, 5.3mmol), to give the title compound(1.1g, 59%).

R_f=0.25(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.65(m, 3H), 7.52(s, 1H), 7.20(t, 2H), 7.10(d, 2H), 6.92(s, 1H), 5.20(s, 2H), 3.80(s, 2H), 2.80(t, 2H), 2.60(t, 2H)

Preparation Example 20

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(3-chloro-pyridin-4-yl)methylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(1.0g, 4.5mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(0.34g, 5.4mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 3-chloropyridine-4-carboxaldehyde(0.64g, 4.5mmol), to give the title compound(0.82g, 52%).

R_f=0.25(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 8.50(s, 1H), 8.40(d, 2H), 7.60(d, 2H), 7.52(s, 1H), 7.30(d, 1H), 7.10(d, 2H), 6.92(s, 1H), 5.20(s, 2H), 3.82(s, 2H), 2.85(t, 2H), 2.62(t, 2H)

Preparation Example 21

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(quinolin-4-yl)methylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(1.0g, 4.5mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(0.34g, 5.4mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 4-quinolinecarboxaldehyde(0.71g, 4.5mmol), to give the title compound(0.81g, 49%).

R_f=0.25(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 8.85(d, 1H), 8.15(d, 1H), 8.05(d, 1H), 7.75(t, 1H), 7.60(d, 2H), 7.52(s, 1H), 7.40(d, 1H), 7.10(d, 2H), 6.98(s, 1H), 5.20(s, 2H), 4.25(s, 2H), 3.00(t, 2H), 2.65(t, 2H)

Preparation Example 22

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(naphthyl-1-yl)methylamin e

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(0.70g, 3.1mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(0.23g, 3.7mmol) and replacing 2-(trifluoromethyl)benzaldehyde with 1-naphthaldehyde(0.48g, 3.1mmol), to give the title compound(0.58g, 51%).

R_f=0.25(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 8.03(dd, 1H), 7.86(dd, 1H), 7.78(dd, 1H), 7.50(d, 4H), 7.42(d, 2H), 7.38(s, 1H), 7.00(d, 2H), 6.90(s, 1H), 5.08(s, 2H), 4.20(s, 2H), 2.90(t, 2H), 2.60(t, 2H)

Preparation Example 23

Synthesis of N-[2-(1-Methyl-1H-imidazol-5-yl)]ethyl-2-trifluoromethylbenzylamine

<Step 1>

2-(1-Methyl-1H-imidazol-5-yl)ethyl phthalimide

To a solution of N-[2-(1-triphenylmethyl-imidazol-4-yl)]ethyl phthalimide(10.0g, 20.7mmol) prepared from <Step 2> of Preparation Example 1 in acetone(100ml) was added dimethyl sulfate(2.2ml, 22.7mmol). The reaction mixture was stirred for overnight at room temperature. The solid of reaction mixture was filtered and washed by ethyl ether(50ml) to give the title compound(4.8g, 90%)

R_f=0.20(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 9.00(s, 1H), 7.85(s, 4H), 7.50(s, 1H), 3.90(s, 6H), 3.40(s, 2H), 3.05(t, 2H)

<Step 2>

2-(1-Methyl-1H-imidazol-5-yl)ethylamine

Hydrazine $2H_2O$(1.5ml, 30.0mmol) was added to a solution of 2-(1-methyl-1H-imidazol-5-yl)ethyl phthalimide(4.8g, 15.0mmol) in 50ml of methanol. The reaction mixture was refluxed for 3hr. The reaction mixture was concentrated *in vacuo*, crystallized with ethyl alcohol(5ml) to give the title compound(1.8g, 95%) as a solid.

^{1}H-NMR(DMSO-d_6) δ 7.50(s, 1H), 6.70(s, 1H), 3.55(s, 3H), 2.85(t, 2H),

2.70(t, 2H)

<Step 3>

N-[2-(1-Methyl-1H-imidazol-5-yl)]ethyl-2-trifluoromethylbenzylamine

To a solution of 2-(1-methyl-1H-imidazol-5-yl)ethylamine(630mg, 5.0mmol) in methanol(10ml) were added 2-(trifluoromethyl)benzaldehyde(870mg, 5.0mmol), AcOH(0.1ml) and molecular sieve(3Å, 1g). The reaction mixture was stirred for 1hr at room temperature. Sodium cyanoborohydride(380mg, 6.0mmol) was added dropwise under ice-water bath. The reaction mixture was stirred for 8hr at room temperature. The insoluble material was filtered off by filtration, and the mother liquid was concentrated *in vacuo*. The residue was dissolved in 20ml of ethyl acetate, and washed with water, saturated $NaHCO_3$ solution. The organic phase was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The resulting residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol = 10/1, v/v) to give the title compound(320mg, 22.6%).

R_f=0.20(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.45-7.65(m, 3H), 7.38(s, 1H), 7.34(t, 1H), 6.80(s, 1H), 4.00(s, 2H), 3.58(s, 3H), 2.90(t, 2H), 2.70(t, 2H)

Preparation Example 24

Synthesis of N-[2-(1-Methyl-1H-imidazol-5-yl)]ethyl-2,3-dichlorobenzylamine

The reaction was carried out under the same condition as described in <Step 3> of Preparation Example 23, using 2-(1-methyl-1H-imidazol-5-yl)ethylamine(630mg, 5.0mmol) prepared from <Step 2> of Preparation Example 23 and sodium cyanoborohydride(380mg, 6.0mmol) and replacing

2-(trifluoromethyl)benzaldehyde with 2,3-dichlorobenzaldehyde(870mg, 5.0mmol), to give the title compound(320mg, 23%).

R_f=0.20(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.28-7.40(m, 4H), 6.80(s, 1H), 3.96(s, 2H), 3.58(s, 3H), 2.90(t, 2H), 2.75(t, 2H)

Preparation Example 25

Synthesis of N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-2-trifluoromethylbenzylamine

<Step 1>

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl phthalimide

To a solution of N-[2-(1-triphenylmethyl-imidazol-4-yl)]ethyl phthalimide(16.2g 33.5mmol) prepared from <Step 2> of Preparation Example 1 in 150ml of acetonitrile was added piperonyl bromide(7.2g, 33.5mmol). The reaction mixture was stirred at 60℃ for overnight. The reaction mixture was concentrated *in vacuo* and dissolved with 150ml of methanol. The reaction mixture was refluxed for 2hr, cooled to room temperature. The resulting solid was filtered and washed by ethyl ether to give the title compound(9.1g, 72%) as a white solid.

R_f=0.30(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 9.20(s, 1H), 7.85(s, 4H), 7.60(s, 1H), 7.00(s, 1H), 6.90(s, 2H), 6.00(s, 2H), 5.40(s, 2H), 3.80(t, 2H), 2.95(t, 2H)

<Step 2>

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethylamine

To a solution of N-{2-[1-(3,4-methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl phthalimide(9.1g, 24.2mmol) in methanol(50ml) was added hydrazine hydrate(2.4ml, 48.5mmol). The reaction mixture was refluxed for 3hr. The reaction mixture was concentrated *in vacuo* to give the title compound(5.38g, 98%) as a solid.

^{1}H-NMR(DMSO-d_6) δ 7.72(s, 1H), 6.90(d, 1H), 6.75(d, 2H), 6.60(d, 1H), 6.60(s, 2H), 5.05(s, 2H), 2.87(t, 2H), 2.70(t, 2H)

<Step 3>

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-2-trifluoromethylbenzylamine

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethylamine(700mg, 2.8mmol) was reacted with 2-(trifluoromethyl)benzaldehyde(500mg, 2.8mmol) under the same condition as described in <Step 5> of Preparation Example 1 to give the title compound(400mg, 35%).

R_f=0.20(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.60(d, 1H), 7.55(m, 2H), 7.35(m, 1H), 6.88(s, 1H), 6.75(d, 1H), 6.55(s, 2H), 6.00(s, 2H), 5.00(s, 2H), 3.95(s, 2H), 2.85(t, 2H), 2.65(t, 2H)

Preparation Example 26

Synthesis of N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-2,3-dichlorobenzylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, but

N-{2-[1-(3,4-methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethylamine(700mg, 2.8mmol) prepared from <Step 2> of Preparation Example 25 reacting with 2,3-dichlorobenzaldehyde(500mg, 2.8mmol) instead of 2-(trifluoromethyl)benzaldehyde, to give the title compound(350mg, 31%).

R_f=0.20(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.50(s, 1H), 7.40(dd, 1H), 7.20(m, 2H), 6.90(s, 1H), 6.75(d, 1H), 6.50(s, 2H), 5.98(s, 2H), 5.00(s, 2H), 3.85(s, 2H), 2.80(t, 2H), 2.65(t, 2H)

Preparation Example 27

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-butylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(700mg, 3.1mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(230mg, 3.7mmol) and replacing 2-(trifluoromethyl)benzaldehyde with butyraldehyde(230mg, 3.7mmol), to give the title compound(240mg, 27%).

R_f=0.10(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.55(s, 1H), 7.15(d, 2H), 6.90(s, 1H), 5.20(s, 2H), 2.80(m, 2H), 2.60(t, 2H), 2.50(d, 1H), 2.00(t, 1H), 1.35(m, 2H), 0.90(m, 5H)

Preparation Example 28

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-isobutylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(700mg,

3.1mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(230mg, 3.7mmol) and replacing 2-(trifluoromethyl)benzaldehyde with isobutyraldehyde(0.28ml, 3.1mmol), to give the title compound(170mg, 19%).

R_f=0.10(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.62(d, 2H), 7.48(s, 1H), 7.10(d, 2H), 6.86(s, 1H), 5.20(s, 2H), 2.82(t, 2H), 2.60(t, 2H), 2.38(d, 2H), 1.70(m, 1H), 0.85(d, 6H)

Preparation Example 29

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-pentylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(700mg, 3.1mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(230mg, 3.7mmol) and replacing 2-(trifluoromethyl)benzaldehyde with valeraldehyde(0.33ml, 3.1mmol), to give the title compound(630mg, 69%).

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H0, 7.50(s, 1H), 7.10(d, 2H), 6.90(s, 1H), 5.20(s, 2H), 2.80(m, 3H), 2.60(m, 3H), 1.30(m, 4H), 0.90(m, 5H)

Preparation Example 30

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-butenylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(700mg, 3.1mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(230mg, 3.7mmol) and replacing

2-(trifluoromethyl)benzaldehyde with crotonaldehyde(0.26ml, 3.1mmol), to give the title compound(420mg, 48%).

^{1}H-NMR($CDCl_3$) δ 7.65(d, 2H), 7.50(d, 1H), 7.10(d, 2H), 6.90(d, 1H), 5.20(s, 2H), 3.25(m, 2H), 2.40-2.65(m, 6H), 1.10(t, 3H)

Preparation Example 31

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-cyclohexylmethylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(700mg, 3.1mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(230mg, 3.7mmol) and replacing 2-(trifluoromethyl)benzaldehyde with cyclohexanecarboxaldehyde(0.38ml, 3.1mmol), to give the title compound(750mg, 75%).

R_f=0.10(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.70(d, 2H), 7.58(s, 1H), 7.20(d, 2H), 7.00(s, 1H), 5.25(s, 2H), 2.85(t, 2H), 2.65(t, 2H), 2.50(d, 2H)1.80(m, 5H), 1.25(m, 4H), 0.95(m, 2H)

Preparation Example 32

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-propylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, using N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(700mg, 3.1mmol) prepared from <Step 4> of Preparation Example 1 and sodium cyanoborohydride(230mg, 3.7mmol) and replacing 2-(trifluoromethyl)benzaldehyde with propionaldehyde(0.22ml, 3.1mmol), to

give the title compound(440mg, 53%).

R_f=0.05(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.40(s, 1H), 7.05(d, 2H), 6.90(s, 1H), 5.18(s, 2H), 2.70(m, 2H), 2.50(m, 2H), 2.25(m, 1H), 1.95(m, 1H), 1.20(m, 2H), 0.80(t, 3H)

Preparation Example 33

Synthesis of N-{2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]}ethyl-2-trifluoromethyl-benzylamine

<Step 1>

N-{2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]}ethyl phthalimide

The reaction was carried out under the same condition as described in <Step 1> of Preparation Example 25, but N-[2-(1-triphenylmethyl-imidazol-4-yl)]ethyl phthalimide(15.5g 32.1mmol) prepared from <Step 2> of Preparation Example 1 reacting with 4-nitrobenzyl bromide(6.9g, 32.1mmol) instead of piperonyl bromide, to give the title compound(8.3g, 69%).

R_f=0.30(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 9.30(s, 1H), 8.23(d, 2H), 7.85(s, 4H), 7.70(s, 1H), 7.60(d, 2H), 5.75(s, 2H), 3.80(t, 2H), 2.95(t, 2H)

<Step 2>

2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]ethylamine

Using the same method as described in <Step 2> of Preparation Example 25, N-{2-[1-(4-nitrobenzyl)-1H-imidazol-5-yl]}ethyl phthalimide(8.3g, 22.1mmol) was transformed to the title compound(5.4g,

99%).

^{1}H-NMR(DMSO-d_6) δ 8.20(d, 2H), 7.80(s, 1H), 7.30(d, 2H), 6.85(s, 1H), 5.40(s, 2H), 2.83(t, 2H), 2.63(t, 2H)

<Step 3>

N-{2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]}ethyl-2-trifluoromethylbenzylamine

2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]ethylamine(700mg, 2.8mmol) was reacted with 2-(trifluoromethyl)benzaldehyde(500mg, 2.8mmol) under the same condition as described in <Step 5> of Preparation Example 1 to give the title compound(440mg, 39%).

R_f=0.20(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 8.20(d, 2H), 7.63(d, 1H), 7.55(m, 3H), 7.37(m, 1H), 7.16(d, 1H), 6.95(s, 1H), 5.20(s, 2H), 3.92(s, 2H), 2.85(t, 2H), 2.60(t, 2H)

Preparation Example 34

Synthesis of N-{2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]}ethyl-2,3-dichloro-benzylamine

The reaction was carried out under the same condition as described in <Step 5> of Preparation Example 1, but 2-[1-(4-nitrobenzyl)-1H-imidazol-5-yl]ethylamine(700mg, 2.8mmol) prepared from <Step 2> of Preparation Example 33 reacting with 2,3-dichlorobenzaldehyde(500mg, 2.8mmol) instead of 2-(trifluoromethyl)benzaldehyde, to give the title compound(400mg, 35%).

R_f=0.20(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 8.20(d, 2H), 7.57(s, 1H), 7.40(dd, 1H), 7.12-7.22(m, 4H), 6.95(s, 1H), 5.20(s, 2H), 3.85(s, 2H), 2.80(t, 2H), 2.60(t, 2H)

Preparation Example 35

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(α-methyl-3-chloro)benzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(0.5g, 2.21mmol) prepared from <Step 4> of Preparation Example 1, AcOH(0.1ml), sodium cyanoborohydride(0.21g, 3.32mmol) and molecular sieve(3Å, 1g) in 30ml of methanol was added 3'-chloroacetophenone(0.34g, 2.21mmol) at 0℃. The reaction mixture was stirred for 3hr at room temperature. The reaction mixture was filtered through celite, and mother liquid was concentrated *in vacuo*. The residue was dissolved in 50ml of dichloromethane and washed with water(50ml). The organic phase was dried over anhydrous magnesium sulfate and concentrated *in vacuo*. The resulting residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(56mg, 7%).

^{1}H-NMR($CDCl_3$) δ 6.88-7.63(m, 10H), 5.12(s, 2H), 3.65(dd, 1H), 2.47-2.73(m, 4H), 1.28(dd, 3H)

Preparation Example 36

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(α-methyl-3-fluoro)benzylamine

The reaction was carried out under the same condition as described in Preparation Example 35, but N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine 2HCl(0.5g, 2.21mmol) prepared from <Step 4> of Preparation Example 1 reacting with 3'-fluoroacetophenone(0.27g, 2.21mmol) instead of 3'-chloroacetophenone, to give the title compound(87mg, 11%).

^{1}H-NMR($CDCl_3$) δ 6.92-7.63(m, 10H), 5.12(s, 2H), 3.65(dd, 1H),

2.47-2.73(m, 4H), 1.28(dd, 3H).

Preparation Example 37

Synthesis of N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-2-trifluoromethylbenzylamine

<Step 1>

3-(1H-Imidazol-4-yl)-acrylic acid methyl ester HCl

The suspension of urocanic acid(100g) in 1000ml of absolute methanol was bubbled by HCl gas for 30minute under ice-water bath. The reaction mixture was refluxed for 1hr and poured into 2000ml of ethyl ether. The resulting solid was filtered and dried *in vacuo* to give the title compound(140g) as a white solid.

R_f=0.3(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 9.24(s, 1H), 8.06(s, 1H), 7.58(d, 1H), 6.94(d, 1H), 3.72(s, 3H)

<Step 2>

3-(1H-Imidazol-4-yl)-propionic acid methyl ester HCl

To a suspension of 3-(1H-imidazol-4-yl)-acrylic acid methyl ester HCl(140g) and Pd-C(10%, 3g) in MeOH(1500ml) was hydrogenated for 48hr. The reaction mixture was filtered and the filtrate was concentrated *in vacuo* to give the title compound(152g).

^{1}H-NMR(DMSO-d_6) δ 9.03(s, 1H), 7.41(s, 1H), 3.60(s, 3H), 2.94(t, 2H), 2.75(t, 2H)

<Step 3>

3-(1-Triphenylmethyl-1H-imidazol-4-yl)-propionic acid methyl ester

To a solution of 3-(1H-imidazol-4-yl)-propionic acid methyl ester HCl(152.4g, 0.80mol) and triethylamine(234ml, 1.68mol) in dimethylformamide(760ml) was added a solution of triphenylmethyl chloride(234g, 0.84mol) in dimethylformamide(990ml) under ice-water bath. After stirring for 18hr at room temperature, water(10L) was added to reaction mixture. The resulting solid was filtered and washed with ethyl ether(2L), dried *in vacuo* to give the title compound(257g, 81%).

R_f=0.4(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 7.30-7.36(m, 10H), 7.25(s, 1H), 7.11-7.18(m, 5H), 6.56(s, 1H), 3.63(s, 3H), 2.89(t, 2H), 2.67(s, 2H)

<Step 4>

3-(1-Triphenylmethyl-1H-imidazol-4-yl)-propanol

To a suspension of lithium aluminium hydride(49.2g, 1.30mol) in absolute tetrahydrofuran(2000ml) was added 3-(1-triphenylmethyl-1H-imidazol-4-yl)-propionic acid methyl ester(257g, 0.65mol) under ice-water bath. The reaction mixture was stirred for 1hr at same temperature and added 100ml of water. The insoluble material was filtered off and the filtrate was concentrated *in vacuo*. The resulting residue was diluted with ethyl acetate(500ml), and washed with water. The organic layer was dried over anhydrous magnesium sulfate, concentrated *in vacuo* to give the title compound(202g, 85%).

R_f=0.3(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.27-7.36(m, 10H), 7.11-7.18(m, 6H), 6.56(s, 1H), 3.74(t, 2H), 2.69(t, 2H), 1.84-1.94(m, 2H)

<Step 5>

3-(1-Triphenylmethyl-1H-imidazol-4-yl)-propyl methanesulfonate

To a solution of 3-(1-triphenylmethyl-1H-imidazol-4-yl)-propanol(202g, 0.55mol) and triethylamine(82.2ml, 0.60mol) in dichloromethane(1000ml) was added dropwise methanesulfonyl chloride(42.3ml, 0.55mol) in dichloromethane(50ml) under ice-water bath. The reaction mixture was stirred for 18hr at room temperature. The reaction mixture was washed with saturated sodium bicarbonate solution. The organic layer was dried over anhydrous sodium sulfate, concentrated *in vacuo* to give the title compound(250g).

R_f=0.4(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.27-7.40(m, 10H), 7.12-7.19(m, 6H), 6.59(s, 1H), 4.25(t, 2H), 2.96(s, 3H), 2.67(t, 2H), 2.13-2.02(m, 2H)

<Step 6>

4-(3-Azido-propyl)-1-triphenylmethyl-1H-imidazole

To a solution of 3-(1-triphenylmethyl-1H-imidazol-4-yl)-propyl methane-sulfonate(250g, 0.56mol) in HMPA(700ml) was added sodium azide(72.8g, 1.12mol). The reaction mixture was heated for 20hr at 60℃. The reaction mixture was extracted with ethyl acetate, washed with water and brine. The organic layer was dried over anhydrous sodium sulfate, concentrated *in vacuo* to give the title compound(206g, 94%).

R_f=0.4(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.27-7.40(m, 10H), 7.15-7.22(m, 6H), 6.58(s, 1H), 3.24(s, 3H), 2.64(t, 2H), 1.87-1.98(m, 2H)

<Step 7>

5-(3-Azido-propyl)-1-(4-cyanobenzyl)-1H-imidazole

To a solution of

4-(3-azido-propyl)-1-triphenylmethyl-1H-imidazole(206g, 0.52mol) in acetonitrile(1000ml) was added 4-cyanobenzyl bromide(91.9g, 0.47mol). The reaction mixture was heated for 18hr at 65℃. The solvent was concentrated *in vacuo* and the resulting residue was diluted with methanol(1000ml). The reaction mixture was heated for 2hr at 80℃.

The solution was concentrated *in vacuo* to the volume of 500 ml and the insoluble material was filtered off. The filtrate was concentrated *in vacuo* and the solid was washed with ethyl acetate, dried *in vacuo* to give the title compound as a solid(147.8g, 81%).

R_f=0.3(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 9.28(s, 1H), 7.91(d, 2H), 7.64(s, 1H), 7.48(d, 2H), 5.61(s, 2H), 3.35(t, 2H), 2.55(t, 2H), 1.65-1.77(m, 2H)

<Step 8>

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-2-trifluoromethylbenzylamine

To a solution of 5-(3-azido-propyl)-1-(4-cyanobenzyl)-1H-imidazole(1.0g, 3.76mmol) and 2-(trifluoromethyl)benzaldehyde(0.51ml, 3.76mmol) in anhydrous tetrahydrofuran(50ml) was added triphenylphosphine(1.0g, 3.76mmol) at 0℃. The reaction was stirred for overnight at room temperature, concentrated *in vacuo* and dissolved in methanol(50ml). Sodium borohydride(0.17g, 4.51mmol) was added dropwise at 0℃. The reaction mixture was stirred for 30 minute at room temperature, concentrated *in vacuo* and partitioned with dichloromethane(50ml) and water(50ml). The organic layer was dried over anhydrous sodium sulfate, concentrated *in vacuo*. The residue *was* purified by silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(1.04g, 69%).

^{1}H-NMR($CDCl_3$) δ 6.88-7.65(m, 10H), 5.17(s, 2H), 3.89(s, 2H), 2.66(t, 2H),

2,45(t, 2H), 1.78(m, 2H).

Preparation Example 38

Synthesis of N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-2,3-dichlorobenzyl-amine

The reaction was carried out under the same condition as described in <Step 8> of Preparation Example 37, but 5-(3-azido-propyl)-1-(4-cyanobenzyl)-1H-imidazole(1.0g, 3.76mmol) prepared from <Step 7> of Preparation Example 37 reacting with 2,3-dichlorobenzaldehyde(0.67ml, 3.76mmol) instead of 2-(trifluoromethyl)benzaldehyde, to give the title compound(1.0g, 67%).
^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.49(s, 1H), 7.35-7.40(m, 1H), 7.20-7.26(m, 2H),7.07(d, 2H), 6.91(s, 1H), 5.18(s, 2H), 3.87(s, 2H), 2.66(t, 2H), 2,39(t, 2H), 1.73-1.81(m, 2H)

Preparation Example 39

Synthesis of N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-3-chlorobenzyl-amine

The reaction was carried out under the same condition as described in <Step 8> of Preparation Example 37, but 5-(3-azido-propyl)-1-(4-cyanobenzyl)-1H-imidazole(1.0g, 3.76mmol) prepared from <Step 7> of Preparation Example 37 reacting with 3-chlorobenzaldehyde(0.44ml, 3.76mmol) instead of 2-(trifluoromethyl)benzaldehyde, to give the title compound(0.76g, 55%).
^{1}H-NMR($CDCl_3$) δ 7.61(d, 2H), 7.50(s, 1H), 7.22-7.27(m, 3H), 7.05-7.13(m, 3H), 6.91(s, 1H), 5.19(s, 2H), 3.91(s, 2H), 2.62(t, 2H), 2,44(t, 2H), 1.71-1.82(m, 2H)

Preparation Example 40

Synthesis of N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-2-methylbenzylamine

The reaction was carried out under the same condition as described in <Step 8> of Preparation Example 37, but 5-(3-azido-propyl)-1-(4-cyanobenzyl)-1H-imidazole(1.0g, 3.76mmol) prepared from <Step 7> of Preparation Example 37 reacting with o-tolualdehyde(0.45ml, 3.76mmol) instead of 2-(trifluoromethyl)benzaldehyde, to give the title compound(0.40g, 31%).

^{1}H-NMR($CDCl_3$) δ 7.61(d, 2H), 7.49(s, 1H), 7.36-7.41(m, 1H), 7.20-7.26(m, 2H),7.07(d, 2H), 6.91(s, 1H), 5.17(s, 2H), 3.89(s, 2H), 2.66(t, 2H), 2,45(t, 2H), 2.29(s, 3H), 1.74-1.82(m, 2H)

Preparation Example 41

Synthesis of N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-(1-naphthyl)methylamine

The reaction was carried out under the same condition as described in <Step 8> of Preparation Example 37, but 5-(3-azido-propyl)-1-(4-cyanobenzyl)-1H-imidazole(1.0g, 3.76mmol) prepared from <Step 7> of Preparation Example 37 reacting with 1-naphthaldehyde(0.52ml, 3.76mmol) instead of 2-(trifluoromethyl)benzaldehyde, to give the title compound(0.63g, 44%).

^{1}H-NMR($CDCl_3$) δ 8.02(dd, 1H), 7.83(dd, 1H), 7.79(dd, 1H), 7.50(d, 4H), 7.42(d, 2H), 7.38(s, 1H), 7.00(d, 2H), 6.68(s, 1H), 5.20(s, 2H), 3.88(s, 2H), 2.67(t, 2H), 2,45(t, 2H), 1.74-1.82(m, 2H)

Preparation Example 42

Synthesis of

N-{4-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}butyl-2-trifluoromethylbenzylamine

<Step 1>

(1-Triphenylmethyl-1H-imidazol-4-yl)carboxaldehyde

To a solution of 4-(hydroxymethyl)imidazole HCl(5.0g, 37.2mmol) and triethylamine(11.4ml, 81.7mmol) in dimethylformamide(50ml) was added triphenylmethyl chloride(11.4g, 40.9mmol) in dimethylformamide(50ml) under ice-water bath. After stirring for 36hr at room temperature, water(1500ml) was added to the reaction mixture. The resulting solid was filtered and suspended with ethyl acetate(200ml) for 1hr. The resulting solid was filtered and dried *in vacuo* to give 1-(triphenylmethyl)-4-(hydroxymethyl)-imidazole(12.2g, 97%) as a white solid. To a solution of 1-(triphenylmethyl)-4-(hydroxymethyl)-imidazole(6.0g, 14.7mmol) in dimethylsulfoxide(75ml) was added sulfur trioxide pyridine complex(5.85g, 36.7mmol) under ice-water bath. After stirring for 3hr at room temperature, water and ethyl acetate were added to the reaction mixture and separated. The organic phase was dried over anhydrous sodium sulfate and concentrated *in vacuo*. The resulting solid was washed with ethyl ether, dried *in vacuo* to give the title compound(4.02g, 81%).

R_f=0.6(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 9.87(s, 1H), 7.61(s, 1H), 7.53(s, 1H), 7.35-7.38(m, 10H), 7.08-7.13(m, 5H)

<Step 2>

N-[4-(1-Triphenylmethyl-1H-imidazol-4-yl)]-3-butenyl-phthalimide

To a solution of N-(3-bromopropyl)-phthalimide(10.7g, 40mmol) in acetonitrile(100ml) was added triphenylphosphine(10.5g, 40mmol), and the

reaction mixture was refluxed for 20hr. The reaction mixture was concentrated *in vacuo*. The resulting solid was washed with water and ethyl ether, dried *in vacuo* to give the 3-(N-phthalimido)propyl-triphenylphosphonium bromide(18.3g, 86%). To a solution of (1-triphenylmethyl-1H-imidazol-4-yl)carboxaldehyde(4.49g, 13.3mmol) prepared from <Step 1> and 3-(N-phthalimido)propyl-triphenylphosphonium bromide(7.77g, 14.6mmol) in anhydrous tetrahytrofuran(100ml) was added potassium t-butoxide(1.79g, 15.9mmol). The reaction mixture was stirred for 3hr at 60℃. The solvent was concentrated *in vacuo* and the resulting solid was washed with ethyl acetate, dried *in vacuo* to give the title compound(6.65g, 98%).

R_f=0.3(EtOAc/n-hexane= 2/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.80-7.86(m, 2H), 7.70-7.76(m, 2H), 7.31-7.39(m, 10H), 7.13-7.18(m, 6H), 6.78(s, 1H), 6.32(d, 1H), 5.50-5.63(m, 1H), 3.86(t, 2H), 2.88-2.99(m, 2H)

<Step 3>

N-[4-(1-Triphenylmethyl-1H-imidazol-4-yl)]butyl phthalimide

To a suspension of N-[4-(1-triphenylmethyl-1H-imidazol-4-yl)]-3-butenyl-phthalimide(3.0g, 5.89mmol) and Pd-C(10%, 0.3g) in tetrahydrofuran/MeOH(120ml, tetrahydrofuran/MeOH=5/1, v/v) was hydrogenated for 3.5hr. The reaction mixture was filtered and filtrate was concentrated *in vacuo* to give the title compound(2.8g, 93%).

^{1}H-NMR($CDCl_3$) δ 7.81-7.86(m, 2H), 7.68-7.73(m, 2H), 7.29-7.34(m, 10H), 7.11-7.16(m, 6H), 6.52(s, 1H), 3.68(t, 2H), 2.58(t. 2H), 1.67-1.70(m, 4H)

<Step 4>

N-{4-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}butyl phthalimide

A suspension of N-[2-(1-triphenylmethyl-imidazol-4-yl)]butyl phthalimide(2.80g, 5.47mmol) and 4-cyanobenzyl bromide(1.07g, 5.47mmol) in acetonitile(30ml) was stirred for 5hr at 65°C. The reaction mixture was concentrated *in vacuo* to give an oily material. After the addition of methanol(40ml), the reaction mixture was heated for 1.5hr at 80℃. The solution was concentrated *in vacuo* and the residue was dissolved dichloromethane. The mixture was washed with saturated solution of sodium bicarbonate and dried over anhydrous magnesium sulfate and concentrated *in vacuo*. The residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give a white solid of the title compound(1.38g, 66%).

^{1}H-NMR($CDCl_3$) δ 7.56-7.67(m, 4H), 7.50-7.53(m, 2H), 7.58(d, 2H), 7.47(s, 1H), 7.09(d, 2H), 6.87(s, 1H), 5.14(s, 2H), 3.63(t, 2H), 2.42(t, 2H), 1.52-1.73(m, 4H)

<Step 5>

1-(4-Cyanobenzyl)-5-(4-aminobutyl)imidazole

To a solution of N-{4-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}butyl phthalimide(1.38g, 3.59mmol)) in ethanol(30ml) was added hydrazine hydrate(0.52g, 10.8mmol). After refluxing for 3hr, the insoluble material was filtered off by filtration. The filtrate was concentrated *in vacuo* and dichloromethane(40ml) was added. The insoluble material was filtered off and the filtrate was concentrated *in vacuo* to give a solid of the title compound(0.86g, 95%).

R_f=0.1(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.47(s, 1H), 7.07(d, 2H), 6.86(s, 1H), 5.12(s, 2H), 2.63(t, 2H), 2.33(t, 2H), 1.42-1.61(m, 6H)

<Step 6>

N-{4-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}butyl-2-trifluoromethylbenzylamine

1-(4-Cyanobenzyl)-5-(4-aminobutyl)imidazole(864mg, 3.4mmol) was reacted with 2-(trifluoromethyl)benzaldehyde(0.45ml, 3.40mmol) under the same condition as described in <Step 5> of Preparation Example 1 to give the title compound(150mg, 11%).

R_f=0.2(dichloromethane/methanol= 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.56-7.67(m, 4H), 7.50-7.53(m, 2H), 7.58(d, 2H), 7.47(s, 1H), 7.09d, 2H), 6.87(s, 1H), 5.14(s, 2H), 3.63(t, 2H), 2.42(t, 2H), 1.52-1.73(m, 4H)

Preparation Example 43

Synthesis of N-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]methyl-2-trifluoromethyl-benzylamine

<Step 1>

1-(Triphenylmethyl)-4-hydroxymethyl-1H-imidazole

Using the same method as described in <Step 2> of Preparation Example 1, 4-(hydroxymethyl)imidazole HCl(5.0g) was transformed to the title compound(12g) as a white solid.

^{1}H-NMR($CDCl_3$) δ 7.4(s, 1H), 7.3-7.4(m, 9H), 7.1-7.2(m, 6H), 6.8(s, 1H), 4.6(s, 2H)

<Step 2>

1-(Triphenylmethyl)-4-acetoxymethyl-1H-imidazole

To a solution of 1-(triphenylmethyl)-4-hydroxymethyl-1H-imidazole(12g, 35.25mmol) in pyridine(50ml) was added acetic anhydride(10ml, 105.75mmol) and the reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with ethyl acetate(400ml) and washed with water(300ml X 3), 10% solution of HCl(50ml) and brine. The organic phase was dried over anhydrous magnesium sulfate and concentrated *in vacuo* to give a white solid of the title compound(6.5g).

^{1}H-NMR($CDCl_3$) δ 7.4(s, 1H), 7.3-7.4(m, 9H), 7.1-7.2(m, 6H), 6.7(s, 1H), 5.0(s, 2H), 2.1(s, 3H)

<Step 3>

1-(4-Cyanobenzyl)-5-acetoxymethyl-1H-imidazole

A suspension of 1-(triphenylmethyl)-4-acetoxymethyl-1H-imidazole(6.5g, 17mmol) and 4-cyanobenzyl bromide(3.7g, 17mmol) in acetonitrile(50ml) were stirred at 50°C for overnight. After the reaction mixture was concentrated *in vacuo,* and methanol(20ml) was added. The reaction mixture was refluxed for 2hr. The solution was concentrated *in vacuo to* give a solid of the title compound(5g).

<Step 4>

1-(4-Cyanobenzyl)-5-hydroxymethyl-1H-imidazole

To a solution of 1-(4-cyanobenzyl)-5-acetoxymethyl-1H-imidazole(5g, 14.9mmol) in tetrahydrofuran(30ml) was added lithium hydroxide monohydrate(1.88g, 44.7mmol) under ice-water bath. After stirring for 1hr at room temperature, the reaction mixture was concentrated *in vacuo*. The residue was diluted with ethyl acetate(100ml) and washed with saturated solution of sodium bicarbonate, water and brine. The organic phase was dried over

anhydrous magnesium sulfate and concentrated *in vacuo to* give the title compound(2.35g, 74%).

R_f=0.1(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.65(d, 2H), 7.52(s, 1H), 7.23(d, 2H), 6.98(s, 1H), 5.35(s, 2H), 4.42(s, 2H)

<Step 5>

1-(4-Cyanobenzyl)-1H-imidzol-5-carboxaldehyde

To a solution of 1-(4-cyanobenzyl)-5-hydroxymethyl-1H-imidazole(0.95g, 4.5mmol) in dimethyl sulfoxide(20ml) were added triethylamine(2.5ml, 18.0mmol) and sulfur trioxide pyridine complex(1.80g, 11.3mmol). After stirring for 1hr at room temperature, the reaction mixture was diluted with ethyl acetate(50ml) and washed with water, brine. The organic phase was dried over anhydrous sodium sulfate and concentrated *in vacuo to* give the title compound. The title compound was used to next step without further purification.

R_f=0.3(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 9.74(s, 1H), 7.87(s, 1H), 7.78(s, 1H), 7.64(d, 2H), 7.26(d, 2H), 5.58(s, 2H)

<Step 6>

N-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]-methyl-2-trifluoromethylbenzylamine

Molecular sieve(3 Å, 0.5g) was added to a solution of 1-(4-cyanobenzyl)-1H-imidzol-5-carboxaldehyde(200mg, 0.95mmol), 2-(trifluoromethyl)benzylamine (170mg, 0.95mmol) and acetic acid(0.1ml) in methanol(10ml). After addition of sodium cyanoborohydride(72mg, 1.2mmol) to above solution, the reaction mixture was stirred for overnight at room

temperature. The reaction mixture was filtered, and the filtrate was concentrated *in vacuo*. The residue was diluted in ethyl acetate(10ml), washed with saturated sodium bicarbonate solution and water. The organic layer was dried over anhydrous magnesium sulfate and concentrated *in vacuo*. The resulting residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(221mg, 63%).

R_f=0.25(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.25-7.65(m, 7H), 7.08(d, 2H), 6.98(s, 1H), 5.35(s, 2H), 3.85(s, 2H), 3.60(s, 2H)

Preparation Example 44

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}acetyl-2-trifluoromethyl-benzylamine

<Step 1>

1H-Imidazol-4-ylacetic acid methyl ester HCl

Hydrogen chloride gas was bubbled through a solution of 4-imidazoleacetic acid HCl(10g) in methanol(200 ml) until saturated. The solution was allowed to stand for 18h at room temperature and then concentrated *in vacuo* to give the title compound(11.6g) as a white solid.

^{1}H-NMR(DMSO-d_6) δ 9.05(s, 1H), 7.50(s, 1H), 3.90(s, 2H), 3.60(s, 3H).

<Step 2>

1-(Triphenylmethyl)-1H-imidazol-4-ylacetic acid methyl ester

To a suspension of 1H-imidazol-4-ylacetic acid methyl ester HCl(11.6 g, 65.6 mmol) in dichloromethane(350 ml) and DMF(50 ml) were added triethylamine(27.4 ml, 196.6 mmol) and triphenylmethyl chloride(21.9 g, 78.6

mmol). The mixture was stirred for 15hr. The reaction mixture was washed with water and brine. The organic layer was dried over anhydrous magnesium sulfate and concentrated *in vacuo* The residue was purified by silica gel column chromatography(eluent: EtOAc/n-hexane=4/1, v/v) to provide a white solid of the title compound(7.4g).

R_f=0.2(EtOAc/n-hexane = 1/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.45(s, 1H), 7.05-7.45(m, 15H), 6.75(s, 1H), 3.70(s, 2H)

<Step 3>

1-(4-Cyanobenzyl)-1H-imidazol-5-ylacetic acid methyl ester

To a solution of 1-triphenylmethyl-1H-imidazol-4-ylacetic acid methyl ester(1.43g, 3.74mmol) in acetonitrile(50 ml) was added 4-cyanobenzyl bromide(0.81g, 4.11mmol) and the mixture was heated to 65°C for 24hr. The reaction mixture was cooled to room temperature and solvent was concentrated *in vacuo*. Methanol(100ml) was added to above residue and heated to reflux temperature for 1hr. The solution was concentrated *in vacuo* to the volume of 10 ml. Crystallization from methanol gave the title compound(0.89g, 93%) as a white solid.

^{1}H-NMR(DMSO-d_6) δ 9.30(s, 1H), 7.95(d, 2H), 7.70(s, 1H), 7.52(d, 2H), 5.65(s, 2H), 3.92(s, 2H), 3.50(s, 3H)

<Step 4>

1-(4-Cyanobenzyl)-1H-imidazol-5-ylacetic acid HCl

A solution of 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid methyl ester(3.3g) in 1.0N HCl(25 ml) was heated at 60°C for 4hr and concentrated *in vacuo* to dryness. The title compound was obtained as a white solid.

^{1}H-NMR(DMSO-d_6) δ 14.60(br, 1H), 12.95(br, 1H), 9.35(s, 1H), 7.95(d, 2H), 7.65(s, 1H), 5.60(s, 2H), 3.80(s, 2H)

<Step 5>

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}acetyl-2-trifluoromethylbenzylamine

To a solution of 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid HCl(3.33g, 0.012mol) and 2-(trifluoromethyl)benzylamine(1.75g, 0.01mol) in dichloromethane(40ml) were added 1-hydroxybenzotriazole(1.62g, 0.012mol), EDAC(2.30g, 0.012mol) and triethylamine(3.51ml, 0.025mol). The reaction mixture was stirred for 18hr at room temperature and washed with saturated sodium bicarbonate solution. The organic layer was dried over anhydrous magnesium sulfate and concentrated *in vacuo*. The residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(1.90g, 47%).

R_f=0.3(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.45-7.71(m, 7H), 7.16(d, 2H), 7.03(s, 1H), 6.18(br, 1H), 5.25(s, 2H), 4.53(d, 1H), 3.44(s, 2H)

Preparation Example 45

Synthesis of N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propionyl-2-trifluoromethylbenzylamine

<Step 1>

3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]propionic acid methyl ester

4-Cyanobenzyl bromide(1.63g, 8.32mmol) was added to a solution of 3-(1-triphenylmethyl-1H-imidazol-4-yl)-propionic acid methyl ester(3.00g, 7.56mmol) prepared from <Step 3> of Preparation Example 37 in ethyl acetate(20ml). The reaction mixture was stirred at 60℃ for 20hr and

concentrated *in vacuo*. Methanol(30ml) was added to the residue and the mixture was stirred for 1hr at 80℃. The reaction mixture was concentrated *in vacuo* to give the title compound(2.32g, 88%).

R_f=0.3(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 9.49(s, 1H), 7.70(d, 2H), 7.67(s, 1H), 7.41(d, 2H), 7.33(s, 1H), 5.66(s, 2H), 3.59(s, 3H), 2.76(t, 2H), 2.58(t, 2H)

<Step 2>

3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]propionic acid HCl

The reaction mixture of 3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]propionic acid methyl ester HBr(1.32g, 3.77mmol) and 4N-HCl(10ml) were stirred for 3hr at 100℃. The solution was concentrated *in vacuo* and the residue was washed with ethyl ether. The solid was dried to give the title compound(1.16g).

R_f=0.3(dichloromethane/methanol = 20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 9.38(s, 1H), 7.91(d, 2H), 7.59(s, 1H), 7.49(d, 2H), 5.69(s, 2H), 2.69(t, 2H), 2.56(t, 2H)

<Step 3>

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propionyl-2-trifluoromethylbenzylamine

To a solution of 3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]propionic acid HCl(1.16g 3.97mmol), triethylamine(1.22ml, 8.73mmol), EDAC(0.91g, 4.76mmol) and 1-hydroxybenzotriazole(0.64g, 4.76mmol) in dichloromethane(30ml) was added 2-(trifluoromethyl)benzylamine(0.63g, 3.57mmol). The reaction mixture was stirred for 18hr at room temperature and washed with saturated sodium bicarbonate solution. The organic layer was dried over anhydrous magnesium sulfate and concentrated *in vacuo*. The

residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(930mg, 57%). ^{1}H-NMR($CDCl_3$) δ 7.72(s, 1H), 7.66(d, 2H), 7.40-7.60(m, 4H), 7.16(d, 2H), 6.90(s, 1H), 6.18(t, 1H), 5.23(s, 2H), 4.63(d, 2H), 2.79(t, 2H), 2.54(t, 2H)

Preparation Example 46

Synthesis of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-methylphenylamine

The reaction mixture of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethylamine(1.33g, 5.00mmol), 2-bromotoluene(0.86g, 5.00mmol), sodium t-butoxide(0.67g, 7.00mmol), tris(dibenzylideneacetone)dipalladium(0)(11.5mg, 0.013mmol) and (S)-(-)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl(23.4mg, 0.036mmol) in toluene(25ml) were stirred for overnight at 90°C through sealed tube reaction. The reaction mixture was poured into ethyl ether(100ml) and the insoluble material was filtered off. The filtrate was concentrated *in vacuo* to give the title compound(684mg, 43%).

Example 1

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-trifluoromethylbenzylamine(120mg, 0.312mmol) prepared from Preparation Example 1 in dichloromethane(10ml) was added 4-methoxyphenyl isothiocyanate(62mg, 0.375mmol). The mixture was stirred for 3hr at room temperature. After concentration *in vacuo,* the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give a

solid(165mg, 96%) of the title compound.

R_f=0.3(dichloromethane/methanol=40/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.75(d, 1H), 7.57-7.64(m, 3H), 7.48-7.52(m, 2H), 7.35(d, 1H), 7.13(d, 2H), 7.03(d, 2H), 6.92(s, 2H), 6.84(d, 2H), 5.44(s, 2H), 4.97(s, 2H), 3.98-4.02(m, 2H), 3.78(s, 3H), 2.99(t, 2H)

Example 2

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-trifluoromethylbenzylamine(120mg, 0.312mmol) prepared from Preparation Example 1 in dichloromethane(10ml) was added 2-methoxypyridin-5-yl isothiocyanate(62.3mg, 0.375mmol). The mixture was stirred for 3hr at room temperature. After concentration *in vacuo,* the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give a solid(122mg, 71%) of the title compound.

R_f=0.3(dichloromethane/methanol=40/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.34-7.80(m, 2H), 7.57-7.61(m, 3H), 7.47-7.53(m, 2H), 7.35(d, 1H), 7.14-7.27(m, 3H), 6.89(s, 1H), 6.71(d, 2H), 5.41(s, 2H), 5.00(s, 2H), 4.00(t, 2H), 3.90(s, 3H), 2.98(t, 2H)

Example 3

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine HCl

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine(675mg) prepared from Example 2

in ethyl acetate(20ml) was bubbled by HCl gas at ice bath. The mixture was diluted with diethyl ether(50ml) and the resulting solid was filtered. The solid was dried *in vacuo* to give the title compound(592mg, 77%).

^{1}H-NMR(CD_3OD) δ 9.04(s, 1H), 8.10-8.18(m, 2H), 7.63-7.80(m, 4H), 7.52-7.59(m, 2H), 7.17-7.43(m, 4H), 5.68(s, 2H), 5.16(s, 2H) 4.07(s, 3H), 4.01(t, 2H), 3.10(t, 2H)

Example 4-39

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-trifluoromethyl-benzylamine prepared from Preparation Example 1 was reacted with the corresponding isothiocyanates under the same condition as described in Example 1 to give the title compounds.

Example 4

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-allylthiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 484

Example 5

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-isobutylthiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 500

Example 6

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxyethyl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.7(d, 1H), 7.5-7.7(d+m, 3H), 7.5(m, 1H), 7.1-7.2(m, 3H), 6.9(s, 1H), 5.4(s, 2H), 4.8(s, 2H), 4.0(m, 2H), 3.7(q, 2H), 3.4(t, 2H), 3.1(s, 3H), 2.9(m, 2H)

LC/MS(MH^+) 502

Example 7

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-ethoxypropyl)thio-carbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 529

Example 8

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(n-butyl)thiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 514

Example 9

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-cyclopentylthio-carbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 512

Example 10

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-cyclohexylthio-carbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 526

Example 11

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.8(d, 1H), 7.6(d, 2H), 7.5(m, 2H), 7.3-7.3(m, 3H), 7.0-7.2(m, 3H), 6.9(m, 3H), 5.4(s, 2H), 5.0(s, 2H), 4.0(m, 2H), 3.0(m, 2H)

LC/MS(MH^+) 538

Example 12

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxyphenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 8.3(d, 1H), 7.6(d+m, 3H), 7.4-7.5(m, 2H), 7.3(m, 1H), 7.2(d, 2H), 7.1(d, 1H), 7.0(m, 2H), 6.8(d, 1H), 5.5(s, 2H), 5.0(s, 2H), 4.0(m, 2H), 3.5(s, 3H), 3.0(m, 2H)

LC/MS(MH^+) 550

Example 13

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylphenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.8(d, 1H), 7.5-7.6(m, 5H), 7.4(d, 1H), 7.1-7.2(m, 4H), 7.0(s, 1H), 6.9-7.0(m, 2H), 5.4(s, 2H), 5.0(s, 2H), 4.0(m, 2H), 3.0(m, 2H), 2.3(s, 3H)

LC/MS(MH^+) 534

Example 14

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-nitrophenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 8.2(d, 2H), 7.8(d, 1H), 7.5-7.6(m, 5H), 7.4(d, 2H), 7.3(d, 1H), 7.2(d, 2H), 7.0(s, 1H), 5.4(s, 2H), 5.0(s, 2H), 4.0(m, 2H), 3.0(t, 2H)

LC/MS(MH^+) 565

Example 15

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-trifluoromethyl-phenyl)thiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 588

Example 16

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methyl-phenyl)thiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 568

Example 17

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-benzylthiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 534

Example 18

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-phenylphenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 596

Example 19

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-chlorophenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 554

Example 20

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[2-(N",N"-dimethyl-amino)ethyl]thiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 515

Example 21

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-trifluoromethoxy-phenyl)-thiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 604

Example 22

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-hydroxy-4-methoxyphenyl)-thiocarbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.7(d, 1H), 7.5-7.6(m, 4H), 7.3(d, 1H), 7.1(d, 2H), 6.9(d, 2H), 6.8(d,1H), 6.6-6.7(m, 2H), 5.4(s, 2H), 5.0(s, 2H), 4.0(m, 2H), 3.9(s, 3H), 3.0(m, 2H)

LC/MS(MH^+) 566

Example 23

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylthiophenyl)-thiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 566

Example 24

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(naphthyl-1-yl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.7-7.8(m, 4H), 7.5-7.6(m, 5H), 7.3-7.5(m, 4H), 7.3(s, 1H), 7.1(d, 2H), 7.0(s, 1H), 5.4(s, 2H), 5.0(s, 2H), 4.0(m, 2H), 3.0(m, 2H)

LC/MS(MH^+) 570

Example 25

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2,2-dimethyl-3,3-dimethyl-butyl)thiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 556

Example 26

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-phenylethyl)thio-carbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 548

Example 27

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-phenylthiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 520

Example 28

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(t-butyl)thiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 500

Example 29

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(n-butyl)thiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 500

Example 30

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(n-propyl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.7(d, 1H), 7.5-7.6(d+m, 4H), 7.4(d, 1H), 7.3(s, 1H), 7.2(d, 2H), 6.9(s, 1H), 5.5(s, 2H), 4.8(s, 2H), 4.0(m, 2H), 3.5(q, 2H), 2.9(m, 2H), 1.4(q, 2H), 0.7(t, 3H)

LC/MS(MH^+) 486

Example 31

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-ethylthiocarbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.7(d, 1H), 7.5-7.6(d+m, 4H), 7.5(d, 1H), 7.1-7.3(d+m, 3H), 6.9(s, 1H), 5.5(s, 2H), 4.8(s, 2H), 3.9(dd, 2H), 3.5(q, 2H), 2.9(m, 2H), 1.0(t, 3H)

LC/MS(MH) 472

Example 32

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-adamantylthio-carbamoy

l-2-trifluoromethylbenzylamine

LC/MS(MH^+) 578

Example 33

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-methylthiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 458

Example 34

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-hydroxyphenyl)-thiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 536

Example 35

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-benzoylthiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 548

Example 36

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-pyrimidyl)thio-carbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 522

Example 37

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(1-piperidino)thio-carbamoyl-2-trifluoromethylbenzylamine

R_f=0.3(dichloromethane/methanol=40/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.0-7.6(m, 9H), 6.8(s, 1H), 5.4(s, 2H), 4.9(s, 2H), 3.7(t, 2H), 3.2(t, 2H), 2.8(m, 4H), 1.6-2.0(m, 6H)

LC/MS(MH^+) 527

Example 38

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-morpholino)thio-carbamoyl-2-trifluoromethylbenzylamine

R_f=0.3(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.1-7.8(m, 9H), 6.9(s, 1H), 5.4(s, 2H), 4.9(s, 2H), 3.6-4.0(m, 4H), 3.0-3.4(m, 4H), 2.4-2.9(m, 4H)

LC/MS(MH^+) 529

Example 39

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methyl-1-piperazino)-thiocarbamoyl-2-trifluoromethylbenzylamine

R_f=0.2(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.0-7.8(m, 9H), 6.8(s, 1H), 5.4(m, 2H), 4.9(s, 2H), 3.7(m, 2H), 2.4-3.3(m, 6H), 2.0-2.2(m, 3H)

LC/MS(MH^+) 542

Example 40

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-trifluoromethyl-benzyl)morpholin-4-carbothioamide

To a solution of morpholine(1.57ml, 18mmol) in chloroform(21.9ml) was added triethylamine(5.17ml, 36mmol) and the reaction mixture was stirred for 30minute at room temperature. A solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-trifluoromethylbenzylamine(500mg, 1.30mmol) prepared from Preparation Example 1 in chloroform(10ml) was added dropwise to the reaction mixture and the mixture was heated at 60℃ for 24hr. After concentration *in vacuo,* the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound.

R_f=0.3(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.18-7.78(m, 10H), 5.78(s, 2H), 4.78(s, 2H), 3.42-3.83(m, 10H), 2.84(t, 2H)

LC/MS(MH^+) 514

Example 41

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxy-phenyl)thiocarbamoyl-2,3-dichlorobenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2,3-dichlorobenzylamine(115mg, 0.32mmol) prepared from Preparation Example 2 in dichloromethane(10ml) was added 4-methoxyphenyl isothiocyanate(58mg, 0.35mmol). The mixture was stirred for 3hr at room temperature. After concentration *in vacuo,* the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give a solid(164mg, 99%) of the title compound.

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.50-7.53(m, 2H), 7.27-7.34(m, 2H), 7.04-7.18(m, 5H), 6.90(d, 2H), 6.84(s, 1H), 5.46(s, 2H), 4.84(s, 2H), 3.95-4.03(m, 2H), 3.81(s, 3H), 2.97-3.05(m, 2H)

LC/MS(MH^+) 550

Example 42

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2,3-dichlorobenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2,3-dichlorobenzylamine(115mg, 0.32mmol) prepared from Preparation Example 2 in dichloromethane(10ml) was added 2-methoxypyridin-5-yl isothiocyanate(60mg,

0.35mmol). The mixture was stirred for 3hr at room temperature. After concentration *in vacuo,* the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give a solid(154mg, 94%) of the title compound.

^{1}H-NMR($CDCl_3$) δ 7.83(d, 1H), 7.60(d, 2H), 7.46-7.52(m, 2H), 7.34(t, 1H), 7.06-7.26(m, 3H), 6.91(s, 1H), 6.72(d, 2H), 5.43(s, 2H), 4.85(s, 2H), 3.94-4.03(m, 2H), 3.91(s, 3H), 2.95-3.03(m, 2H)

LC/MS(MH^+) 551

Example 43-55

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2,3-dichlorobenzyl-amine prepared from Preparation Example 2 was reacted with the corresponding isothiocyanates under the same condition as described in Example 41 to give the title compounds.

Example 43

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)thio-carbamoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.63-7.54(m, 2H), 7.38-7.50(m, 3H), 7.22-7.38(m, 2H), 6.99-7.18(m, 4H), 6.85-6.96(m, 2H), 5.41(s, 2H), 4.81(s, 2H), 3.94(t, 2H), 2.95(t, 2H)

LC/MS(MH^+) 538

Example 44

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-chlorophenyl)thio-carbamoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.43-7.59(m, 3H), 7.24-7.33(m, 4H), 7.07-7.11(m, 5H), 6.84(s, 1H), 5.39(s, 2H), 4.81(s, 2H), 3.93(t, 2H), 2.95(t, 2H)

LC/MS(MH^+) 554

Example 45

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylphenyl)thio-carbamoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.31-7.59(m, 4H), 7.24-7.31(m, 2H), 6.99-7.14(m, 6H), 6.89(s, 1H), 5.42(s, 2H), 4.81(s, 2H), 3.95(t, 2H), 2.97(t, 2H), 2.31(s, 3H)

LC/MS(MH^+) 534

Example 46

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-nitrophenyl)thio-carbamoyl-2,3-dichlorobenzylamine

LC/MS(MH^+) 565

Example 47

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methyl-phenyl)thiocarbamoyl-2,3-dichlorobenzylamine

LC/MS(MH^+) 568

Example 48

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)-thiocarbamoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.46-7.59(m, 4H), 7.24-7.32(m, 2H), 6.94-7.17(m, 5H), 6.85(s, 1H), 5.40(s, 2H), 4.81(s, 2H), 3.93(t, 2H), 2.96(t, 2H), 2.31(s, 3H)

LC/MS(MH^+) 554

Example 49

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylthiophenyl)-thiocarbamoyl-2,3-dichlorobenzylamine

LC/MS(MH^+) 566

Example 50

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-cyclohexylthio-carbamoyl-2,3-dichlorobenzylamine

LC/MS(MH^+) 526

Example 51

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-ethoxycarbonyl-thiocarbamoyl-2,3-dichlorobenzylamine

LC/MS(MH^+) 516

Example 52

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(naphthyl-2-yl)thio-carbamoyl-2,3-dichlorobenzylamine

LC/MS(MH^+) 570

Example 53

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-phenylthiocarbamoyl-2,3-dichlorobenzylamine

LC/MS(MH^+) 520

Example 54

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methylphenyl)thio-carbamoyl-2,3-dichlorobenzylamine

LC/MS(MH^+) 534

Example 55

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-fluorophenyl)thio-carbamoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.46-7.60(m, 4H), 7.21-7.32(m, 2H), 6.94-7.13(m, 6H), 6.86(s, 1H), 5.40(s, 2H), 4.81(s, 2H), 3.93(t, 2H), 2.96(t, 2H)

LC/MS(MH^+) 535

Example 56

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-chlorophenyl)thio-carbamoyl-2-chlorobenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-chlorobenzylamine(0.02M solution in dichloromethane, 1ml, 0.02mmol) prepared from Preparation Example 3 was added a solution of 4-chlorophenyl isothiocyanate(0.1M in dichloromethame, 0.2ml, 0.02mmol). After stirring for 2hr at room temperature, the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound as a white foam.

^{1}H-NMR($CDCl_3$) δ 7.58(d, 2H), 7.43-7.47(m, 2H), 7.18-7.36(m, 4H), 7.08-7.14(m, 4H), 6.88(s, 1H), 5.41(s, 2H), 4.81(s, 2H), 3.97(t, 2H), 2.96(t, 2H)
LC/MS(MH^+) 520

Example 57-59

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-chlorobenzyl-amine prepared from Preparation Example 3 was reacted with the corresponding isothiocyanates under the same condition as described in Example 56 to give the title compounds.

Example 57

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methyl-phenyl)thio-carbamoyl-2-chlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.51-7.63(m, 4H), 7.26-7.34(m, 2H), 7.12-7.18(m,4H), 6.91-6.99(m, 3H), 5.43(s, 2H), 4.80(s, 2H), 3.93(t, 2H), 2.98(t, 2H), 2.32(s, 3H)

LC/MS(MH^+) 534

Example 58

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-2-chlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.59(s, 1H), 7.57(d, 2H), 7.42-7.47(m, 2H), 7.25-7.35(m, 3H), 7.01-7.07(m, 3H), 6.81-6.91(m, 3H), 5.41(s, 2H), 4.81(s, 2H), 3.98(t, 2H), 3.77(s, 3H), 2.98(t, 2H)

LC/MS(MH^+) 516

Example 59

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-2-chlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.81(s, 1H), 7.58(d, 2H), 7.42-7.52(m, 3H), 7.31-7.36(m, 2H), 7.11-7.27(m, 3H), 6.89(s, 1H), 6.90(d, 1H), 5.43(s, 2H), 4.83(s, 2H), 4.01(t, 2H), 3.89(s, 3H), 2.96(t, 2H)

LC/MS(MH^+) 517

Example 60

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)thio-carbamoyl-3-chlorobenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-3-chlorobenzylamine(0.02M solution in dichloromethane, 2ml, 0.04mmol) prepared from Preparation Example 4 was added a solution of 3-fluorophenyl isothiocyanate(0.1M solution in dichloromethane, 0.4ml, 0.04mmol). After stirring for 2hr at room temperature, the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound as a white foam.

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.50(s, 1H), 7.35(m, 2H), 7.18-7.30(m, 3H), 7.00-7.16(m, 4H), 6.80-6.97(m, 3H), 5.40(s, 2H), 4.79(s, 2H), 4.00(dd, 2H), 2.95(dd, 2H)

LC/MS(MH^+) 504

Example 61-67

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-3-chlorobenzyl-amine prepared from Preparation Example 4 was reacted with the corresponding isothiocyanates under the same condition as described in Example 60 to give the title compounds.

Example 61

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-bromophenyl)thio-carbamoyl-3-chlorobenzylamine

LC/MS(MH^+) 564

Example 62

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylphenyl)thio-carbamoyl-3-chlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.50(s, 1H), 7.35(m, 1H), 7.26(s, 1H), 6.98-7.22(m, 9H), 6.91(s, 1H), 5.41(s, 2H), 4.78(s, 2H), 4.00(dd, 2H), 2.95(dd, 2H), 2.32(s, 3H)

LC/MS(MH^+) 500

Example 63

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methyl-phenyl)-thiocarbamoyl-3-chlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.52(s, 1H), 7.35(m, 2H), 7.06-7.22(m, 6H), 6.91-7.02(m, 3H), 5.41(s, 2H), 4.78(s, 2H), 4.00(dd, 2H), 2.95(dd, 2H), 2.32(s,

3H)

LC/MS(MH^+) 534

Example 64

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)thiocarbamoyl-3-chlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.50(s, 1H), 7.35(m, 2H), 7.01-7.27(m, 9H), 6.90(s, 1H), 5.39(s, 2H), 4.79(s, 2H), 4.00(dd, 2H), 2.95(dd, 2H)

LC/MS(MH^+) 520

Example 65

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-trifluoromethyl-phenyl)-thiocarbamoyl-3-chlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.50(s, 1H), 7.35(m, 2H), 7.11-7.25(m, 9H), 6.92(s, 1H), 5.40(s, 2H), 4.80(s, 2H), 4.02(dd, 2H), 2.95(dd, 2H)

LC/MS(MH^+) 570

Example 66

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-3-chlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.52(s, 1H), 7.34(m, 2H), 7.00-7.26(m, 7H), 6.86(t, 3H), 5.41(s, 2H), 4.78(s, 2H), 4.00(dd, 2H), 3.78(s, 3H), 2.95(dd, 2H)

LC/MS(MH^+) 516

Example 67

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-3-chlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.78(d, 1H), 7.60(d, 2H), 7.50(m, 2H), 7.36(m, 2H), 7.21(s, 1H), 7.09-7.16(m, 4H), 6.91(s, 1H), 6.70(d, 1H), 5.40(s, 2H), 4.80(s, 2H), 4.03(dd, 2H), 3.90(s, 3H), 2.95(dd, 2H)

LC/MS(MH^+) 517

Example 68

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)thio-carbamoyl-2-fluorobenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-fluorobenzylamine(0.02M solution in dichloromethane, 1ml, 0.02mmol) prepared from Preparation Example 5 was added a solution of 3-fluorophenyl isothiocyanate(0.1M solution in dichloromethane, 0.2ml, 0.02mmol). After stirring for 3hr at room temperature, the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound as a white foam.

^{1}H-NMR($CDCl_3$) δ 7.61(s, 1H), 7.53(d, 2H), 7.03-7.38(m, 7H), 6.89-6.91(m, 4H), 5.41(s, 2H), 4.80(s, 2H), 3.99(t, 2H), 2.94(t, 2H)

LC/MS(MH^+) 488

Example 69-73

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-fluorobenzyl-amine prepared from Preparation Example 5 was reacted with the corresponding isothiocyanates under the same condition as described in Example 68 to give the title compounds.

Example 69

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylphenyl)thio-carbamoyl-2-fluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.59(s, 1H), 7.53(d, 2H), 7.32-7.38(m, 1H), 7.06-7.22(m, 9H), 5.42(s, 2H), 4.80(s, 2H), 3.99(t, 2H), 2.94(t, 2H), 2.45(s, 3H)

LC/MS(MH^+) 484

Example 70

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methyl-phen
yl)thiocarbamoyl-2-fluorobenzylamine

LC/MS(MH^+) 518

Example 71

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylthiophenyl)-thi
ocarbamoyl-2-fluorobenzylamine

LC/MS(MH^+) 516

Example 72

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-c
arbamoyl-2-fluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.60(s, 1H), 7.54(d, 2H), 7.31-7.37(m, 1H), 7.04-7.21(m, 7H), 6.88(d, 2H), 6.82(s, 1H), 5.43(s, 2H), 4.80(s, 2H), 4.00(t, 2H), 3.78(s, 3H), 2.95(t, 2H)

LC/MS(MH^+) 500

Example 73

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)t
hio-carbamoyl-2-fluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.82(s, 1H), 7.48-7.60(m, 4H), 7.34-7.37(m, 1H), 7.10-7.27(m, 5H), 6.89(s, 1H), 6.70(d, 1H), 5.40(s, 2H), 4.81(s, 2H), 4.00(t, 2H), 3.89(s, 3H), 2.93(t, 2H)

LC/MS(MH^+) 501

Example 74

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-fluorophenyl)thio-car

bamoyl-3-fluorobenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-3-fluorobenzylamine(0.02M solution in dichloromethane, 2ml, 0.04mmol) prepared from Preparation Example 6 was added a solution of 4-fluorophenyl isothiocyanate(0.1M solution in dichloromethane, 0.4ml, 0.04mmol). The mixture was stirred for 2hr at room temperature. The reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound as a white foam.

^{1}H-NMR($CDCl_3$) δ 7.62(d, 2H), 7.54(s, 1H), 7.34-7.48(m, 1H), 7.18(s, 1H), 6.98-7.14(m, 8H), 6.95(s, 1H), 5.45(s, 2H), 4.83(s, 2H), 4.06(t, 2H), 3.00(t, 2H)

LC/MS(MH^+) 488

Example 75-81

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-3-fluorobenzyl-amine prepared from Preparation Example 6 was reacted with the corresponding isothiocyanates under the same condition as described in Example 74 to give the title compounds.

Example 75

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylphenyl)thio-carbamoyl-3-fluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.62(s, 1H), 7.55(d, 2H), 7.35-7.42(m, 1H), 7.12-7.17(m, 5H), 6.99-7.05(m, 4H), 6.93(s, 1H), 5.44(s, 2H), 4.81(s, 2H), 4.05(t, 2H), 2.98(t, 2H), 2.34(s, 3H)

LC/MS(MH^+) 484

Example 76

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methylpheny
l)-thiocarbamoyl-3-fluorobenzylamine
^{1}H-NMR($CDCl_3$) δ 7.62(s, 1H), 7.54(d, 2H), 7.34-7.41(m, 1H), 7.05-7.17(m, 4H), 6.92-7.00(m, 5H), 6.93(s, 1H), 5.41(s, 2H), 4.78(s, 2H), 4.00(t, 2H), 2.97(t, 2H), 2.32(s, 3H)
LC/MS(MH^+) 518

Example 77
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)thio-car
bamoyl-3-fluorobenzylamine
^{1}H-NMR($CDCl_3$) δ 7.62(s, 1H), 7.53(d, 2H), 7.36-7.41(m, 1H), 6.98-7.23(m, 9H), 6.92(s, 1H), 5.40(s, 2H), 4.79(s, 2H), 4.02(t, 2H), 2.95(t, 2H)
LC/MS(MH^+) 504

Example 78
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-c
arbamoyl-3-fluorobenzylamine
^{1}H-NMR($CDCl_3$) δ 7.61(s, 1H), 7.53(d, 2H), 7.34-7.45(m, 1H), 6.99-7.16(m, 4H), 6.81-6.92(m, 3H), 5.43(s, 2H), 4.80(s, 2H), 4.04(t, 2H), 3.81(s, 3H), 2.97(t, 2H)
LC/MS(MH^+) 500

Example 79
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)t
hiocarbamoyl-3-fluorobenzylamine
^{1}H-NMR($CDCl_3$) δ 7.77(d, 1H), 7.60(d, 2H), 7.35-7.50(m, 3H), 6.97-7.15(m, 5H), 6.73(s, 1H), 6.71(d, 1H), 5.41(s, 2H), 4.82(s, 2H), 4.05(t, 2H), 3.90(s, 3H), 2.96(t, 2H)
LC/MS(MH^+) 501

Example 80

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylthiophenyl)-thiocarbamoyl-3-fluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.60(s, 1H), 7.53(d, 2H), 7.34-7.41(m, 1H), 7.10-7.19(m, 9H), 6.90(s, 1H), 5.40(s, 2H), 4.78(s, 2H), 4.01(t, 2H), 2.90(t, 2H), 2.44(s, 3H)

LC/MS(MH^+) 516

Example 81

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-trifluoromethyl-phenyl)thiocarbamoyl-3-fluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.60(s, 1H), 7.52(d, 2H), 7.37-7.43(m, 5H), 6.97-7.14(m, 5H), 6.90(s, 1H), 5.39(s, 2H), 4.82(s, 2H), 4.03(t, 2H), 2.95(t, 2H)

LC/MS(MH^+) 538

Example 82

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methylphenyl)-thiocarbamoyl-2-methylbenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-methylbenzylamine(0.02 M solution in dichloromethane, 1ml, 0.02mmol) prepared from Preparation Example 7 was added a solution of 3-chloro-4-methylphenyl isothiocyanate(0.1M solution in dichloromethane, 0.2ml, 0.02mmol). The mixture was stirred for 2hr at room temperature. The reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound.

^{1}H-NMR($CDCl_3$) δ 7.61(s, 1H), 7.53(d, 2H), 7.26-7.28(m, 3H), 7.07-7.16(m, 4H), 6.90-6.96(m, 3H), 5.46(s, 2H), 4.66(s, 2H), 4.02(t, 2H), 2.98(t, 2H), 2.31(s, 3H), 2.28(s, 3H)

LC/MS(MH^+) 514

Example 83-89

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-methylbenzyl-amine prepared from Preparation Example 7 was reacted with the corresponding isothiocyanates under the same condition as described in Example 82 to give the title compounds.

Example 83

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-fluorophenyl)thio-carbamoyl-2-methylbenzylamine

LC/MS(MH^+) 484

Example 84

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)thio-carbamoyl-2-methylbenzylamine

LC/MS(MH^+) 484

Example 85

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylphenyl)thio-carbamoyl-2-methylbenzylamine

LC/MS(MH^+) 480

Example 86

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-trifluoromethyl-phenyl)thiocarbamoyl-2-methylbenzylamine

LC/MS(MH^+) 534

Example 87

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)-thiocar

bamoyl-2-methylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.59(d, 1H), 7.49(s, 1H), 7.26-7.31(m, 3H), 7.00-7.22(m, 7H), 6.89(s, 1H), 5.44(s, 2H), 4.67(s, 2H), 4.01(t, 2H), 2.98(t, 2H), 2.28(s, 3H)

LC/MS(MH^+) 500

Example 88

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-2-methylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.57(d, 1H), 7.52(s, 1H), 7.25(s, 3H), 7.00-7.16(m, 5H), 6.80-6.91(m, 3H), 5.46(s, 2H), 4.67(s, 2H), 4.03(t, 2H), 3.77(s, 3H), 2.99(t, 2H), 2.28(s, 3H)

LC/MS(MH^+) 496

Example 89

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-2-methylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.76(d, 1H), 7.58(d, 2H), 7.44-7.49(m, 2H), 7.25-7.29(m, 2H), 7.06-7.14(m, 5H), 6.87(s, 1H), 6.69(d, 1H), 5.44(s, 2H), 4.70(s, 2H), 4.03(t, 2H), 3.88(s, 3H), 2.97(t, 2H), 2.28(s, 3H)

LC/MS(MH^+) 497

Example 90

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)thio-carbamoyl-2,3-difluorobenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2,3-difluorobenzylamine(0.02M solution in dichloromethane, 2ml, 0.04mmol) prepared from Preparation Example 8 was added a solution of 3-fluorophenyl isothiocyanate(0.1M solution in dichloromethane, 0.4ml, 0.04mmol). The mixture was stirred for 3hr

at room temperature and purified by short silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound as a white foam.

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.51(s, 1H), 7.36(s, 1H), 7.02-7.20(m, 8H), 6.92(s, 1H), 5.39(s, 2H), 4.87(s, 2H), 3.96(t, 2H), 2.94(t, 2H)

LC/MS(MH^+) 506

Example 91-97

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2,3-difluorobenzyl-amine prepared from Preparation Example 8 was reacted with the corresponding isothiocyanates under the same condition as described in Example 90 to give the title compounds.

Example 91

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-fluorophenyl)thio-carbamoyl-2,3-difluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.59(d, 2H), 7.50(s, 1H), 7.32(s, 1H), 7.00-7.16(m, 8H), 6.90(s, 1H), 5.39(s, 2H), 4.87(s, 2H), 3.96(t, 2H), 2.94(t, 2H)

LC/MS(MH^+) 506

Example 92

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylphenyl)thio-carbamoyl-2,3-difluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.53-7.61(m, 3H), 7.26(s, 1H), 7.01-7.15(m, 8H), 6.93(s, 1H), 5.41(s, 2H), 4.86(s, 2H), 3.97(t, 2H), 2.95(t, 2H), 2.33(s, 3H)

LC/MS(MH^+) 502

Example 93

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methyl-phen

yl)thiocarbamoyl-2,3-difluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.59(d, 2H), 7.53(s, 1H), 7.27(s, 1H), 7.12-7.18(m, 4H), 6.94-7.01(m, 4H), 5.41(s, 2H), 4.86(s, 2H), 3.96(t, 2H), 2.94(t, 2H), 2.34(s, 3H)

LC/MS(MH^+) 536

Example 94

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)-thiocarbamoyl-2,3-difluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.51(s, 1H), 7.31(s, 3H), 6.99-7.27(m, 8H), 6.92(s, 1H), 5.39(s, 2H), 4.87(s, 2H), 3.95(t, 2H), 2.94(t, 2H)

LC/MS(MH^+) 522

Example 95

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-trifluoromethyl-phenyl)thio-carbamoyl-2,3-difluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.61(d, 2H), 7.54(s, 1H), 7.00-7.27(m, 9H), 6.95(s, 1H), 5.40(s, 2H), 4.88(s, 2H), 3.98(t, 2H), 2.95(t, 2H)

LC/MS(MH^+) 572

Example 96

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-2,3-difluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.59(d, 2H), 7.51(s, 1H), 7.00-7.22(m, 7H), 6.89(d, 2H), 6.83(s, 1H), 5.41(s, 2H), 4.87(s, 2H), 3.96(t, 2H), 3.79(s, 3H), 2.95(t, 2H)

LC/MS(MH^+) 518

Example 97

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-2,3-difluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 8.84(d, 1H), 7.61(d, 2H), 7.48-7.53(m, 2H), 7.39(s, 1H),

6.99-7.22(m, 4H), 6.89(s, 1H), 6.72(d, 1H), 5.40(s, 2H), 4.89(s, 2H), 3.98(t, 2H), 3.91(s, 3H), 2.95(t, 2H)
LC/MS(MH^+) 519

Example 98

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylphenyl)thio-carbamoyl-2,6-difluorobenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2,6-difluorobenzylamine(0.02M solution in dichloromethane, 2ml, 0.04mmol) prepared from Preparation Example 9 was added a solution of 4-methylphenyl isothiocyanate(0.1M solution in dichloromethane, 0.4ml, 0.04mmol). The mixture was stirred for 4hr at room temperature and purified by short silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound as a white foam.
^{1}H-NMR($CDCl_3$) δ 7.53-7.66(m, 4H), 7.37-7.40(m, 1H), 6.95-7.17(m, 9H), 5.44(s, 2H), 4.76(s, 2H), 3.98(t, 2H), 2.91(t, 2H), 2.36(s, 1H)
LC/MS(MH^+) 502

Example 99-102

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2,6-difluorobenzyl-amine prepared from Preparation Example 9 was reacted with the corresponding isothiocyanates under the same condition as described in Example 98 to give the title compounds.

Example 99

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-fluorophenyl)thio-carbamoyl-2,6-difluorobenzylamine

LC/MS(MH^+) 506

Example 100

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methyl-phenyl)thiocarbamoyl-2,6-difluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.63(s, 1H), 7.56(d, 2H), 7.39-7.43(m, 1H), 7.25-7.32(m, 2H), 7.01-7.21(m, 5H), 6.97(s, 1H), 5.44(s, 2H), 4.77(s, 2H), 4.00(t, 2H), 2.92(t, 2H), 2.38(s, 3H)

LC/MS(MH^+) 536

Example 101

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-2,6-difluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.62(s, 1H), 7.55(d, 2H), 7.37-7.44(m, 1H), 6.89-7.28(m, 8H), 6.89(s, 1H), 5.45(s, 2H), 4.76(s, 2H), 4.01(t, 2H), 3.83(s, 3H), 2.93(t, 2H)

LC/MS(MH^+) 518

Example 102

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-2,6-difluorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.95(d, 1H), 7.48-7.68(m, 5H), 7.32-7.44(m, 1H), 6.94-7.27(m, 4H), 6.74(d, 1H), 5.41(s, 2H), 4.77(s, 2H), 4.00(t, 2H), 3.92(s, 3H), 2.91(t, 2H)

LC/MS(MH^+) 519

Example 103

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-fluorophenyl)-thiocarbamoyl-4-trifluoromethylbenzylamine

To a solution of

N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-4-trifluoromethylbenzylamine(20mg, 0.05mmol) prepared from Preparation Example 10 in dichloromethane(1ml) was added a solution of 4-fluorophenyl isothiocyanate(0.5M solution in dichloromethane, 0.1ml, 0.05mmol). The mixture was stirred for 4hr at room temperature, and the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(25mg, 94%).

^{1}H-NMR($CDCl_3$) δ 7.69(d, 2H), 7.59(d, 2H), 7.35-7.47(m, 4H), 6.96-7.13(m, 5H), 6.83(s, 1H), 5.41(s, 2H), 4.93(s, 2H), 4.02(t, 2H), 2.95(t, 2H)

LC/MS(MH^+) 538

Example 104-109

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-4-trifluoromethyl-benzylamine prepared from Preparation Example 10 was reacted with the corresponding isothiocyanates under the same condition as described in Example 103 to give the title compounds.

Example 104

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-chlorophenyl)-thiocarbamoyl-4-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.72(d, 2H), 7.60(d, 2H), 7.35-7.49(m, 3H), 7.26-7.30(m, 3H), 7.07-7.13(m, 3H), 6.84(s, 1H), 5.41(s, 2H), 4.93(s, 2H), 4.01(t, 2H), 2.95(t, 2H)

LC/MS(MH^+) 554

Example 105

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methyl-phenyl)thio-carbamoyl-4-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.71(d, 2H), 7.62(d, 2H), 7.53(s, 1H), 7.38(d, 2H),

7.11-7.21(m, 4H), 6.94-6.98(m, 1H), 6.93(s, 1H), 5.44(s, 2H), 4.91(s, 2H), 4.03(t, 2H), 2.98(t, 2H)
LC/MS(MH^+) 568

Example 106
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)-thiocarbamoyl-4-trifluoromethylbenzylamine
^{1}H-NMR($CDCl_3$) δ 7.69(d, 2H), 7.58-7.62(m, 3H), 7.43(s, 1H), 7.36(d, 2H), 7.04-7.25(m, 5H), 6.83(s, 1H), 5.40(s, 2H), 4.93(s, 2H), 4.00(t, 2H), 2.95(t, 2H)
LC/MS(MH^+) 554

Example 107
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-4-trifluoromethylbenzylamine
^{1}H-NMR($CDCl_3$) δ 7.69(d, 2H), 7.60(d, 2H), 7.50(s, 1H), 7.38(d, 2H), 7.13(d, 3H), 7.04(d, 2H), 6.84-6.89(m, 3H), 5.44(s, 2H), 4.91(s, 2H), 4.03(t, 2H), 3.80(s, 3H), 2.98(t, 2H)
LC/MS(MH^+) 550

Example 108
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-4-trifluoromethylbenzylamine
^{1}H-NMR($CDCl_3$) δ 7.80(d, 1H), 7.71(d, 2H), 7.62(d, 2H), 7.46-7.51(m, 2H), 7.39(d, 2H), 7.11-7.19(m, 3H), 6.90(s, 1H), 6.73(d, 1H), 5.43(s, 2H), 4.94(s, 2H), 4.05(t, 2H), 3.92(s, 3H), 2.98(t, 2H)
LC/MS(MH^+) 551

Example 109
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)-thiocarbamoyl-4-trifluoromethylbenzylamine

H-NMR($CDCl_3$) δ 7.72(d, 2H), 7.56-7.62(m, 3H), 7.46(s, 1H), 7.24-7.39(m, 2H), 7.12(d, 2H), 6.99-7.04(m, 1H), 6.73(d, 1H), 6.86-6.91(m, 3H), 5.41(s, 2H), 4.93(s, 2H), 4.01(t, 2H), 2.95(t, 2H)

LC/MS(MH^+) 538

Example 110

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)-thiocarbamoyl-(1-methyl-1H-pyrrol-2-yl)methylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(1-methyl-1H-pyrrol-2-yl)methylamine(15mg, 0.05mmol) prepared from Preparation Example 11 in dichloromethane(1ml) was added a solution of 3-fluorophenyl isothiocyanate(0.5M solution in dichloromethane, 0.1ml, 0.05mmol). The mixture was stirred for 1hr at room temperature and purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(19mg, 90%).

^{1}H-NMR($CDCl_3$) δ 7.85(s, 1H), 7.60(d, 2H), 7.48(s, 1H), 7.25(d, 1H), 7.15(d, 2H), 7.02(t, 1H), 6.80-6.92(m, 3H), 6.70(t, 1H), 6.12(s, 2H), 5.40(s, 2H), 4.75(s, 2H), 4.00(dd, 2H), 3.60(s, 3H), 2.85(dd, 2H)

LC/MS(MH^+) 473

Example 111-114

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(1-methyl-1H-pyrrol-2-yl)methylamine prepared from Preparation Example 11 was reacted with the corresponding isothiocyanates under the same condition as described in Example 110 to give the title compounds.

Example 111

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-chlorophenyl)thio-carbamoyl-(1-methyl-1H-pyrrol-2-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.80(s, 1H), 7.60(d, 2H), 7.48(s, 1H), 7.25(d, 2H), 7.06-7.20(m, 4H), 6.88(s, 1H), 6.70(t, 1H), 6.12(s, 2H), 5.40(s, 2H), 4.75(s, 2H), 4.00(dd, 2H), 3.60(s, 3H), 2.85(dd, 2H)

LC/MS(MH^+) 489

Example 112

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)thio-carbamoyl-(1-methyl-1H-pyrrol-2-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.83(s, 1H), 7.60(d, 3H), 7.48(s, 1H), 7.00-7.25(m, 6H), 6.88(s, 1H), 6.70(t, 1H), 6.12(s, 2H), 5.40(s, 2H), 4.76(s, 2H), 4.00(dd, 2H), 3.60(s, 3H), 2.85(dd, 2H)

LC/MS(MH^+) 489

Example 113

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-(1-methyl-1H-pyrrol-2-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.60(d, 3H), 7.45(s, 1H), 7.00-7.20(m, 4H), 6.85(m, 3H), 6.67(t, 1H), 6.10(s, 2H), 5.40(s, 2H), 4.75(s, 2H), 3.98(dd, 2H), 3.80(s, 3H), 3.58(s, 3H), 2.83(dd, 2H)

LC/MS(MH^+) 485

Example 114

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-(1-methyl-1H-pyrrol-2-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.82(d, 1H), 7.78(s, 1H), 7.60(d, 2H), 7.52(dd, 1H), 7.47(s, 1H), 7.15(d, 2H), 6.87(s, 1H), 6.70(d, 2H), 6.10(d, 2H), 5.40(s, 2H), 4.78(s, 2H), 3.98(dd, 2H), 3.92(s, 3H), 3.58(s, 3H), 2.83(dd, 2H)

LC/MS(MH^+) 486

Example 115

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-fluorophenyl)thio-carbamoyl-(1H-indol-3-yl)methylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(1H-indol-3-yl)methylamine (15mg, 0.04mmol) prepared from Preparation Example 12 in dichloromethane(1ml) was added a solution of 4-fluorophenyl isothiocyanate(0.5M solution in dichloromethane, 0.1ml, 0.05mmol). The reaction mixture was stirred for 2hr at room temperature and purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(21mg, 97%).

^{1}H-NMR($CDCl_3$) δ 9.00(s, 1H), 7.50-7.60(m, 5H), 7.45(d, 1H), 7.18-7.33(m, 2H), 7.02-7.17(m, 5H), 6.98(d, 2H), 6.90(s, 1H), 5.40(s, 2H), 4.97(s, 2H), 4.10(dd, 2H), 3.00(dd, 2H)

LC/MS(MH^+) 509

Example 116-119

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(1H-indol-3-yl)methylamine prepared from Preparation Example 12 was reacted with the corresponding isothiocyanates under the same condition as described in Example 115 to give the title compounds.

Example 116

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)thio-carbamoyl-(1H-indol-3-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 9.07(s, 1H), 7.70(s, 1H), 7.40-7.60(m, 5H), 7.20-7.32(m, 3H), 7.00-7.17(m, 6H), 6.90(s, 1H), 5.40(s, 2H), 4.97(s, 2H), 4.10(dd, 2H),

3.00(dd, 2H)

LC/MS(MH^+) 525

Example 117

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-phenylethyl)thio-carbamoyl-(1H-indol-3-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.60(s, 1H), 7.66(d, 2H), 7.45(d, 2H), 7.25(t, 1H), 7.10-7.20(m, 6H), 7.05(m, 2H), 6.82(d, 2H), 6.15(t, 1H), 5.40(s, 2H), 4.67(s, 2H), 4.00(dd, 2H), 3.82(m, 2H), 2.85(m, 4H)

LC/MS(MH^+) 519

Example 118

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-(1H-indol-3-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 9.00(s, 1H), 7.40-7.60(m, 6H), 7.00-7.32(m, 7H), 6.90(s, 1H), 6.80(d, 2H), 5.40(s, 2H), 4.97(s, 2H), 4.10(dd, 2H), 3.78(s, 3H), 3.00(dd, 2H)

LC/MS(MH^+) 521

Example 119

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-(1H-indol-3-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 9.18(s, 1H), 7.78(d, 1H), 7.65(s, 1H), 7.40-7.60(m, 6H), 7.00-7.32(m, 5H), 6.86(s, 1H), 6.78(d, 1H), 5.40(s, 2H), 4.97(s, 2H), 4.10(dd, 2H), 3.85(s, 3H), 3.00(dd, 2H)

LC/MS(MH^+) 522

Example 120

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)thio-carbamoyl-(6-methyl-pyridin-2-yl)methylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(6-methyl-pyridin-2-yl)methylamine(10mg, 0.03mmol) prepared from Preparation Example 16 in dichloromethane(1ml) was added a solution of 3-fluorophenyl isothiocyanate(0.5M solution in dichloromethane, 72ul, 0.036mmol). The mixture was stirred for 3hr at room temperature. The reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(14mg, 96%).

^{1}H-NMR($CDCl_3$) δ 11.72(s, 1H), 7.65(t, 1H), 7.60(d, 2H), 7.56(s, 1H), 7.10-7.40(m, 7H), 6.96(s, 1H), 6.85(m, 1H), 5.50(s, 2H), 4.60(s, 2H), 3.90(q, 2H), 2.96(q, 2H), 2.60(s, 3H)

LC/MS(MH^+) 485

Example 121-125

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(6-methyl-pyridin-2-yl)methyl-amine prepared from Preparation Example 16 was reacted with the corresponding isothiocyanates under the same condition as described in Example 120 to give the title compounds.

Example 121

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methyl-phenyl)thiocarbamoyl-(6-methyl-pyridin-2-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 11.58(s, 1H), 7.65(t, 1H), 7.60(d, 2H), 7.50(m, 2H), 7.10-7.50(m, 6H), 6.96(s, 1H), 5.50(s, 2H), 4.60(s, 2H), 3.90(q, 2H), 2.96(q, 2H), 2.60(s, 3H), 2.40(s, 3H).

LC/MS(MH^+) 515

Example 122

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)-thiocarbamoyl-(6-methyl-pyridin-2-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 11.72(s, 1H), 7.65(t, 1H), 7.60(d, 2H), 7.56(m, 2H), 7.40(m, 1H), 7.10-7.30(m, 6H), 6.96(s, 1H), 5.50(s, 2H), 4.60(s, 2H), 3.90(q, 2H), 2.96(q, 2H), 2.60(s, 3H)

LC/MS(MH^+) 501

Example 123

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylthio-phenyl)thio-carbamoyl-(6-methyl-pyridin-2-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 11.55(s, 1H), 7.65(t, 1H), 7.60(d, 2H), 7.56(s, 1H), 7.40(m, 2H), 7.40(m, 2H), 7.15(q, 4H), 6.96(s, 1H), 5.50(s, 2H), 4.60(s, 2H), 3.90(q, 2H), 2.96(q, 2H), 2.60(s, 3H), 2.45(s, 3H)

LC/MS(MH^+) 513

Example 124

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-(6-methyl-pyridin-2-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 11.30(s, 1H), 7.65(t, 1H), 7.60(d, 2H), 7.56(s, 1H), 7.26(d, 2H), 7.18(q, 4H), 6.98(s, 2H), 6.90(s, 1H), 5.50(s, 2H), 4.60(s, 2H), 3.95(q, 2H), 3.80(s, 3H), 3.00(q, 2H), 2.60(s, 3H)

LC/MS(MH^+) 497

Example 125

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-(6-methyl-pyridin-2-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 11.45(s, 1H), 8.10(d, 1H), 7.80(dd, 1H), 7.65(t, 1H), 7.60(d, 2H), 7.56(s, 1H), 7.15(q, 7H), 6.96(s, 1H), 6.80(d, 1H), 5.45(s, 2H), 4.62(s, 2H), 4.00(s, 3H), 3.94(q, 2H), 2.98(q, 2H), 2.60(s, 3H)

LC/MS(MH^+) 498

Example 126

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)-thiocarbamoyl-(2-chloro-pyridin-3-yl)methylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(2-chloro-pyridin-3-yl)methylamine(15mg, 0.043mmol) prepared from Preparation Example 18 in dichloromethane(1ml) was added a solution of 3-fluorophenyl isothiocyanate(0.5M solution in dichloromethane, 102ul, 0.051mmol). The mixture was stirred for 1hr at room temperature. The reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(19mg).

^{1}H-NMR($CDCl_3$) δ 8.40(dd, 1H), 7.95(s, 1H), 7.60(m, 3H), 7.42(s, 1H), 7.20-7.40(m, 2H), 7.12(d, 2H), 6.85-7.08(m, 3H), 6.80(s, 1H), 5.40(s, 2H),4.85(s, 2H), 3.95(q, 2H), 2.96(q, 2H)

LC/MS(MH^+) 505

Example 127-128

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(2-chloro-pyridin-3-yl)methylamine prepared from Preparation Example 18 was reacted with the corresponding isothiocyanates under the same condition as described in Example 126 to give the title compounds.

Example 127

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methyl-phenyl)thio-carbamoyl-(2-chloro-pyridin-3-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 8.36(dd, 1H), 7.90(s, 1H), 7.56(m, 3H), 7.40(s, 1H), 7.30(m, 1H), 7.12(m, 4H), 7.00(dd, 1H), 6.80(s, 1H), 5.40(s, 2H), 4.85(s, 2H),

3.90(q, 2H), 2.96(q, 2H), 2.30(s, 3H)
LC/MS(MH^+) 535

Example 128

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-trifluoromethyl-phenyl)thiocarbamoyl-(2-chloro-pyridin-3-yl)methylamine
^{1}H-NMR($CDCl_3$) δ 8.38(dd, 1H), 8.22(s, 1H), 7.80(s, 1H), 7.56(m, 3H), 7.42(s, 4H), 7.32(m, 2H), 7.10(d, 2H), 6.80(s, 1H), 5.40(s, 2H), 4.90(s, 2H), 3.95(q, 2H), 2.96(q, 2H)
LC/MS(MH^+) 555

Example 129

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)-thiocarbamoyl-(1-methyl-1H-indol-3-yl)methylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(1-methyl-1H-indol-3-yl)methylamine(15mg, 0.041mmol) prepared from Preparation Example 13 in dichloromethane(1ml) was added a solution of 3-fluorophenyl isothiocyanate(0.5M solution in dichloromethane, 97ul, 0.05mmol). The reaction mixture was stirred for 1hr at room temperature and purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(20mg).
^{1}H-NMR($CDCl_3$) δ 7.56(m, 5H), 7.36(m, 2H), 7.20(d, 1H), 7.10(m, 4H), 7.00(s, 1H), 6.90(s, 1H), 6.85(m, 2H), 5.40(s, 2H), 4.92(s, 2H), 4.08(dd, 2H), 3.80(s, 3H), 3.00(dd, 2H)
LC/MS(MH^+) 523

Example 130-131

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(1-methyl-1H-indol-3-yl)methylamine prepared from Preparation Example 13 was reacted with the corresponding isothiocyanates under the same condition as described in Example 129 to give the title compounds.

Example 130

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methylphenyl)thio-carbamoyl-(1-methyl-1H-indol-3-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.55(m, 5H), 7.35(m, 2H), 7.20(m, 1H), 7.10(m, 4H), 6.95(m, 2H), 6.87(s, 1H), 5.40(s, 2H), 4.92(s, 2H), 4.08(dd, 2H), 3.80(s, 3H), 3.00(dd, 2H), 2.30(s, 3H)

LC/MS(MH^+) 553

Example 131

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)-thiocarbamoyl-(1-methyl-1H-indol-3-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.55(m, 5H), 7.35(m, 2H), 7.18(m, 6H), 7.00(m, 2H), 6.90(s, 1H), 5.40(s, 2H), 4.92(s, 2H), 4.08(dd, 2H), 3.80(s, 3H), 3.00(dd, 2H)

LC/MS(MH^+) 539

Example 132

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-chlorophenyl)-thiocarbamoyl-(3-chloro-pyridin-4-yl)methylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(3-chloro-pyridin-4-yl)methylamine(12mg, 0.035mmol) prepared from Preparation Example 20 in dichloromethane(1ml) was added a solution of 4-chlorophenyl isothiocyanate(0.5M solution in dichloromethane, 80ul, 0.04mmol). After stirring for 1hr at room temperature, the reaction mixture was purified by short

silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(16mg).

^{1}H-NMR($CDCl_3$) δ 8.60(s, 1H), 8.55(d, 1H), 7.65(s, 1H), 7.60(d, 2H), 7.45(s, 1H), 7.25(m, 2H), 7.10(m, 5H), 6.84(s, 1H), 5.40(s, 2H), 4.90(s, 2H), 3.96(dd, 2H), 2.96(dd, 2H)

LC/MS(MH^+) 521

Example 133-134

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(3-chloro-pyridin-4-yl)methylamine prepared from Preparation Example 20 was reacted with the corresponding isothiocyanates under the same condition as described in Example 132 to give the title compounds.

Example 133

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methylphenyl)thio-carbamoyl-(3-chloro-pyridin-4-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 8.60(s, 1H), 8.55(d, 1H), 7.65(s, 1H), 7.60(d, 2H), 7.42(s, 1H), 7.15(m, 5H), 7.00(m, 1H), 6.84(s, 1H), 5.40(s, 2H), 4.90(s, 2H), 3.96(dd, 2H), 2.96(dd, 2H), 2.35(s, 3H)

LC/MS(MH^+) 535

Example 134

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-(3-chloro-pyridin-4-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 8.55(s, 1H), 8.50(d, 1H), 8.00(s, 1H), 7.80(d, 1H), 7.60(d, 2H), 7.48(dd, 1H), 7.40(s, 1H), 7.10(m, 3H), 6.80(s, 1H), 6.70(d, 1H), 5.40(s, 2H), 4.90(s, 2H), 3.96(dd, 2H), 3.85(s, 3H), 2.96(dd, 2H)

LC/MS(MH^+) 518

Example 135

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)thio-carbamoyl-(2,6-dichloro-pyridin-3-yl)methylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(2,6-dichloro-pyridin-3-yl)methylamine(13.5mg, 0.035mmol) prepared from Preparation Example 17 in dichloromethane(1ml) was added a solution of 3-fluorophenyl isothiocyanate(0.5M solution in dichloromethane, 80ul, 0.04mmol). The mixture was stirred for 1hr at room temperature and purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(19mg).

^{1}H-NMR($CDCl_3$) δ 8.02(s, 1H), 7.60(t, 3H), 7.45(s, 1H), 7.35(d, 1H),7.25(m, 1H), 7.15(d, 2H), 6.89-7.08(m, 3H), 6.82(s, 1H), 5.38(s, 2H), 4.86(s, 2H), 3.95(t, 2H), 2.95(t, 2H)

LC/MS(MH^+) 539

Example 136-139

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(2,6-dichloro-pyridin-3-yl)methylamine prepared from Preparation Example 17 was reacted with the corresponding isothiocyanates under the same condition as described in Example 135 to give the title compounds.

Example 136

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methylphenyl)thio-carbamoyl-(2,6-dichloro-pyridin-3-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 8.00(s, 1H), 7.60(t, 3H), 7.42(s, 1H), 7.35(d, 1H), 7.15(m, 4H), 7.00(dd, 1H), 6.80(s, 1H), 5.38(s, 2H), 4.86(s, 2H), 3.92(t, 2H), 2.95(t, 2H), 2.35(s, 3H)

LC/MS(MH^+) 569

Example 137

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-trifluoromethyl-phenyl)thiocarbamoyl-(2,6-dichloro-pyridin-3-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 8.30(s, 1H), 7.60(t, 3H), 7.43(s, 5H), 7.35(d, 1H), 7.10(d, 2H), 6.80(s, 1H), 5.38(s, 2H), 4.92(s, 2H), 3.95(t, 2H), 2.95(t, 2H)

LC/MS(MH^+) 589

Example 138

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-(2,6-dichloro-pyridin-3-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.60(q, 3H), 7.45(s, 1H), 7.35(d, 1H), 7.10(m, 4H), 6.83(d, 3H), 5.38(s, 2H), 4.86(s, 2H), 3.95(t, 2H), 3.80(s, 3H), 2.95(t, 2H)

LC/MS(MH^+) 551

Example 139

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-(2,6-dichloro-pyridin-3-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 8.22(s, 1H), 7.82(d, 1H), 7.60(d, 2H), 7.50(t, 2H), 7.40(s, 1H), 7.35(d, 1H), 7.10(d, 2H), 6.78(d, 1H), 6.72(d, 1H), 5.38(s, 2H), 4.86(s, 2H), 3.95(t, 2H), 3.88(s, 3H), 2.95(t, 2H)

LC/MS(MH^+) 552

Example 140

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)thio-carbamoyl-(5-methoxy-1H-indol-3-yl)methylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(5-methoxy-1H-indol-3-yl)

methylamine(13.5mg, 0.035mmol) prepared from Preparation Example 15 in dichloromethane(1ml) was added a solution of 3-fluorophenyl isothiocyanate(0.5M solution in dichloromethane, 80ul, 0.04mmol). The mixture was stirred for 3hr at room temperature. And the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(15mg).

^{1}H-NMR($CDCl_3$) δ 8.80(s, 1H), 7.62(s, 1H), 7.55(m, 3H), 7.35(d, 1H), 7.00-7.18(m, 5H), 6.95(d, 3H), 6.82(m, 2H), 5.40(s, 2H), 4.89(s, 2H), 4.08(t, 2H), 3.80(s, 3H), 2.97(t, 2H)

LC/MS(MH^+) 539

Example 141-144

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(5-methoxy-1H-indol-3-yl)methylamine prepared from Preparation Example 15 was reacted with the corresponding isothiocyanates under the same condition as described in Example 140 to give the title compounds.

Example 141

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylphenyl)thio-carbamoyl(5-methoxy-1H-indol-3-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 8.78(s, 1H), 7.50(t, 4H), 7.31(d, 1H), 7.10(m, 5H), 6.96(d, 4H), 6.90(s, 1H), 5.40(s, 2H), 4.89(s, 2H), 4.08(t, 2H), 3.80(s, 3H), 2.97(t, 2H), 2.27(s, 3H)

LC/MS(MH^+) 535

Example 142

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)thio-carbamoyl-(5-methoxy-1H-indol-3-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 8.80(s, 1H), 7.60(d, 2H), 7.52(d, 2H), 7.35(d, 1H),

7.00-7.20(m, 7H), 6.92(d, 3H), 5.40(s, 2H), 4.90(s, 2H), 4.07(t, 2H), 3.80(s, 3H), 2.98(t, 2H)
LC/MS(MH^+) 555

Example 143
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-(5-methoxy-1H-indol-3-yl)methylamine
^{1}H-NMR($CDCl_3$) δ 8.75(s, 1H), 7.55(m, 3H), 7.42(s, 1H), 7.35(d, 1H), 6.92-7.12(m, 7H), 6.90(s, 1H), 6.80(d, 2H), 5.40(s, 2H), 4.90(s, 2H), 4.07(t, 2H), 3.82(s, 3H), 3.76(s, 3H), 2.98(t, 2H)
LC/MS(MH^+) 551

Example 144
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-(5-methoxy-1H-indol-3-yl)methylamine
^{1}H-NMR($CDCl_3$) δ 8.90(s, 1H), 7.75(d, 1H), 7.55(m, 5H), 7.30(d, 1H), 7.08(d, 3H), 6.90(d, 3H), 6.65(d, 1H), 5.40(s, 2H), 4.90(s, 2H), 4.07(t, 2H), 3.85(s, 3H), 3.80(s, 3H), 2.98(t, 2H)
LC/MS(MH^+) 552

Example 145
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)thio-carbamoyl-(2-methyl-1H-indol-3-yl)methylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(2-methyl-1H-indol-3-yl)methylamine(13mg, 0.035mmol) prepared from Preparation Example 14 in dichloromethane(1ml) was added a solution of 3-fluorophenyl isothiocyanate(0.5M solution in dichloromethane, 80ul, 0.04mmol). After stirring for 2hr at room temperature, the reaction mixture was purified by short

silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(14mg).

^{1}H-NMR($CDCl_3$) δ 8.62(s, 1H), 7.75(s, 1H), 7.55(d, 2H), 7.48(s, 1H), 7.43(d, 1H), 7.35(d, 1H), 7.05-7.22(m, 5H), 6.95(m, 1H), 6.80(m, 3H), 5.38(s, 2H), 4.83(s, 2H), 4.00(t, 2H), 2.85(t, 2H), 2.40(s, 3H)

LC/MS(MH^+) 523

Example 146

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methyl-phenyl)thiocarbamoyl-(quinolin-4-yl)methylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(quinolin-4-yl)methylamine (13mg, 0.035mmol) prepared from Preparation Example 21 in dichloromethane(1ml) was added a solution of 3-chloro-4-methylphenyl isothiocyanate(0.5M solution in dichloromethane, 80ul, 0.04mmol). The mixture was stirred for 2hr at room temperature. The reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(17mg).

^{1}H-NMR($CDCl_3$) δ 8.95(d, 1H), 8.20(d, 1H), 7.80(t, 2H), 7.72(s, 1H), 7.62(d, 1H), 7.58(d, 2H), 7.40(s, 1H), 7.20(s, 3H), 7.05(m, 3H), 6.80(s, 1H), 5.39(s, 2H), 5.30(s, 2H), 4.00(t, 2H), 3.00(t, 2H), 2.35(s, 3H)

LC/MS(MH^+) 551

Example 147-148

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(quinolin-4-yl)-methylamine prepared from Preparation Example 21 was reacted with the corresponding isothiocyanates under the same condition as described in Example 146 to give the title compounds.

Example 147

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-phenylethyl)thiocarba moyl-(quinolin-4-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 8.80(d, 1H), 8.20(d, 1H), 7.82(t, 1H), 7.64(m, 2H), 7.59(d, 2H), 7.45(s, 1H), 7.15(d, 2H), 6.90-7.00(m, 7H), 5.43(s, 2H), 4.95(s, 2H), 3.98(t, 2H), 3.85(q, 2H), 2.95(t, 2H), 2.80(t, 2H)

LC/MS(MH^+) 531

Example 148

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)t hio-carbamoyl-(quinolin-4-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 8.92(d, 1H), 8.18(d, 1H), 7.92(s, 1H), 7.87(d, 1H), 7.80(t, 2H), 7.62(m, 1H), 7.57(d, 3H), 7.40(s, 1H), 7.22(d, 1H), 7.10(d, 2H), 6.80(s, 1H), 6.72(d, 1H), 5.38(s, 2H), 5.31(s, 2H), 4.05(t, 2H), 3.85(s, 3H), 3.00(t, 2H)

LC/MS(MH^+) 534

Example 149

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methyl-phen yl)thiocarbamoyl-(6-chloro-pyridin-2-yl)methylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(6-chloro-pyridin-2-yl)meth ylamine(190mg, 0.55mmol) prepared from Preparation Example 19 in dichloromethane(1ml) was added 3-chloro-4-methylphenyl isothiocyanate(110mg, 0.6mmol). The mixture was stirred for 4hr at room temperature, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(270mg).

^{1}H-NMR($CDCl_3$) δ 10.60(s, 1H), 7.80(t, 1H), 7.60(m, 3H), 7.48(s, 1H),

7.40(d, 1H), 7.20-7.40(m, 3H), 7.15(d, 2H), 6.95(s, 1H), 5.42(s, 2H), 4.64(s, 2H), 3.90(dd, 2H), 2.96(dd, 2H), 2.38(s, 3H)
LC/MS(MH^+) 535

Example 150
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)thio-carbamoyl-(naphthyl-1-yl)methylamine

To a solution of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(naphthyl-1-yl)methylamine(13mg, 0.035mmol) prepared from Preparation Example 22 in dichloromethane(1ml) was added a solution of 3-fluorophenyl isothiocyanate(0.5M solution in dichloromethane, 80ul, 0.04mmol). The mixture was stirred for 2hr at room temperature. The mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(16mg).
^{1}H-NMR($CDCl_3$) δ 7.80-8.00(m, 3H), 7.60(m, 2H), 7.50(d, 3H), 7.42(s, 1H), 7.35(s, 1H), 7.25(d, 1H), 7.18(d, 1H), 7.08(d, 2H), 7.00(m, 1H), 6.85(d, 2H), 6.80(s, 1H), 5.40(s, 2H), 5.20(s, 2H), 4.00(dd, 2H), 3.00(dd, 2H)
LC/MS(MH^+) 520

Example 151-155

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(naphthyl-1-yl)methyl-amine prepared from Preparation Example 22 was reacted with the corresponding isothiocyanates under the same condition as described in Example 150 to give the title compounds.

Example 151
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylphenyl)thio-car

bamoyl-(naphthyl-1-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.80-8.00(m, 3H), 7.60(m, 2H), 7.50(d, 3H), 7.45(s, 1H), 7.25(d, 1H), 7.10(p, 7H), 6.82(s, 1H), 5.40(s, 2H), 5.20(s, 2H), 4.00(dd, 2H), 3.00(dd, 2H), 2.30(s, 3H)

LC/MS(MH^+) 516

Example 152

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methyl-phenyl)thio-carbamoyl-(naphthyl-1-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.80-8.00(m, 3H), 7.60(m, 2H), 7.50(m, 3H), 7.40(s, 1H), 7.25(m, 2H), 7.10(m, 7H), 6.97(dd, 1H), 6.80(s, 1H), 5.40(s, 2H), 5.20(s, 2H), 4.00(dd, 2H), 3.00(dd, 2H), 2.30(s, 3H)

LC/MS(MH^+) 550

Example 153

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)thiocarbamoyl-(naphthyl-1-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.80-8.00(m, 3H), 7.60(m, 2H), 7.50(m, 3H), 7.40(s, 1H), 7.36(s, 1H), 7.25(d, 2H), 7.15(m, 2H), 7.05(d, 3H), 6.80(s, 1H), 5.40(s, 2H), 5.20(s, 2H), 4.00(dd, 2H), 3.00(dd, 2H)

LC/MS(MH^+) 536

Example 154

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-(naphthyl-1-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.80-8.00(m, 3H), 7.60(m, 2H), 7.50(d, 3H), 7.42(s, 1H), 7.30(d, 1H), 7.12(d, 2H), 7.05(m, 3H), 6.80(d+s, 3H), 5.40(s, 2H), 5.20(s, 2H), 4.05(dd, 2H), 3.77(s, 3H), 3.00(dd, 2H)

LC/MS(MH^+) 532

Example 155

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-(naphthyl-1-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.80-8.00(m, 4H), 7.60(m, 2H), 7.50(m, 4H), 7.25(d, 2H), 6.80(s, 1H), 6.67(d, 1H), 5.40(s, 2H), 5.20(s, 2H), 4.03(dd, 2H), 3.82(s, 3H), 3.00(dd, 2H)

LC/MS(MH^+) 533

Example 156

N-[2-(1-Methyl-1H-imidazol-5-yl)]ethyl-N-(3-chloro-4-methylphenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

To a solution of N-[2-(1-methyl-1H-imidazol-5-yl)]ethyl-2-trifluoromethyl-benzylamine(11mg, 0.04mmol) prepared from Preparation Example 23 in dichloromethane(1ml) was added a solution of 3-chloro-4-methylphenyl isothiocyanate(0.5M solution in dichloromethane, 88ul, 0.04mmol). The mixture was stirred for 1hr at room temperature. The reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound.

^{1}H-NMR($CDCl_3$) δ 7.75(d, 1H), 7.61(m, 1H), 7.40-7.60(m, 3H), 7.30(s, 1H), 7.10-7.20(m, 2H), 7.00(dd, 1H), 6.79(s, 1H), 5.12(s, 2H), 4.03(dd, 2H), 3.62(s, 3H), 3.09(dd, 2H), 2.32(s, 3H)

LC/MS(MH^+) 467

Example 157

N-[2-(1-Methyl-1H-imidazol-5-yl)]ethyl-N-(3-fluorophenyl)thiocarbamoyl-2,3-dichlorobenzylamine

To a solution of

N-[2-(1-methyl-1H-imidazol-5-yl)]ethyl-2,3-dichlorobenzyl-amine(11mg, 0.04mmol) prepared from Preparation Example 24 in dichloromethane(1ml) was added a solution of 3-fluorophenyl isothiocyanate(0.5M solution in dichloromethane, 88ul, 0.04mmol). The mixture was stirred for 2hr at room temperature. And the mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound.

^{1}H-NMR($CDCl_3$) δ 7.69(s, 1H), 7.47(d, 1H), 7.30(m, 3H), 7.20(t, 1H), 7.07(d, 2H), 6.90(m, 2H), 6.77(s, 1H), 4.97(s, 2H), 4.03(dd, 2H), 3.62(s, 3H), 3.09(dd, 2H)

LC/MS(MH^+) 437

Example 158-159

N-[2-(1-Methyl-1H-imidazol-5-yl)]ethyl-2,3-dichlorobenzylamine prepared from Preparation Example 24 was reacted with the corresponding isothiocyanates under the same condition as described in Example 157 to give the title compounds.

Example 158

N-[2-(1-Methyl-1H-imidazol-5-yl)]ethyl-N-(4-trifluoromethylphenyl)thio-carbamoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.72(s, 1H), 7.47(d, 1H), 7.25(m, 3H), 7.15(m, 4H), 6.72(s, 1H), 4.97(s, 2H), 4.03(dd, 2H), 3.62(s, 3H), 3.09(dd, 2H)

LC/MS(MH^+) 503

Example 159

N-[2-(1-Methyl-1H-imidazol-5-yl)]ethyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.78(d, 1H), 7.50(dd, 1H), 7.35(d, 1H), 7.30(s, 1H),

7.20(t, 2H), 7.05(d, 1H), 6.65(m, 2H), 4.87(s, 2H), 3.97(dd, 2H), 3.80(s, 3H), 3.60(s, 3H), 3.00(dd, 2H)
LC/MS(MH^+) 450

Example 160

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methylphenyl)thiocarbamoyl-2-trifluoromethylbenzylamine

To a solution of N-{2-[1-(3,4-methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-2-trifluoromethylbenzylamine(12mg, 0.03mmol) prepared from Preparation Example 25 in dichloromethane(1ml) was added a solution of 3-chloro-4-methylphenyl isothiocyanate(0.5M solution in dichloromethane, 60ul, 0.03mmol). The mixture was stirred for 3hr at room temperature. The reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(16mg).
^{1}H-NMR($CDCl_3$) δ 7.75(d, 1H), 7.60(m, 1H), 7.47(d, 1H), 7.40(m, 3H), 7.17(d, 2H), 7.00(dd, 1H), 6.82(s, 1H), 6.70(d, 1H), 6.55(m, 2H), 5.90(s, 2H), 5.12(s, 2H), 5.02(s, 2H), 3.97(dd, 2H), 3.00(dd, 2H), 2.35(s, 3H)
LC/MS(MH^+) 587

Example 161-163

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-2-trifluoromethylbenzylamine prepared from Preparation Example 25 was reacted with the corresponding isothiocyanates under the same condition as described in Example 160 to give the title compounds.

Example 161

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-N-(4-flu

oro-phenyl)thiocarbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.75(d, 1H), 7.60(m, 1H), 7.47(d, 1H), 7.40(m, 3H), 7.35(s, 1H), 7.15(m, 2H), 7.00(t, 2H), 6.82(s, 1H), 6.70(d, 1H), 6.55(m, 2H), 5.90(s, 2H), 5.12(s, 2H), 5.02(s, 2H), 3.97(dd, 2H), 3.00(dd, 2H)

LC/MS(MH^+) 557

Example 162

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-N-(4-methyl-phenyl)thiocarbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.75(d, 1H), 7.60(m, 1H), 7.45(m, 3H), 7.00-7.20(m, 5H), 6.87(s, 1H), 6.70(d, 1H), 6.55(m, 2H), 5.90(s, 2H), 5.15(s, 2H), 5.02(s, 2H), 3.98(dd, 2H), 3.00(dd, 2H), 2.32(s, 3H)

LC/MS(MH^+) 553

Example 163

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-N-(4-trifluoro-methylphenyl)thiocarbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.75(d, 1H), 7.60(m, 1H), 7.50(m, 3H), 7.45(m, 2H), 7.35(d, 3H), 6.84(s, 1H), 6.70(d, 1H), 6.55(m, 2H), 5.90(s, 2H), 5.10(s, 2H), 5.05(s, 2H), 3.98(dd, 2H), 3.00(dd, 2H)

LC/MS(MH^+) 607

Example 164

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-N-(4-chloro-phenyl)thiocarbamoyl-2,3-dichlorobenzylamine

To a solution of N-{2-[1-(3,4-methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-2,3-dichlorobenzylamine(12mg, 0.03mmol) prepared from Preparation Example 26 in dichloromethane(1ml) was added a solution of 4-chlorophenyl

isothiocyanate(0.5M solution in dichloromethane, 60ul, 0.03mmol). After stirring for 1hr at room temperature, the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(14mg).

^{1}H-NMR($CDCl_3$) δ 7.60(s, 1H), 7.45(d, 1H), 7.40(s, 1H), 7.25(m, 3H), 7.10(m, 3H), 6.80(s, 1H), 6.70(d, 1H), 6.55(m, 2H), 5.90(s, 2H), 5.10(s, 2H), 4.80(s, 2H), 3.90(dd, 2H), 3.00(dd, 2H)

LC/MS(MH^+) 573

Example 165-169

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-2,3-dichlorobenzylamine prepared from Preparation Example 26 was reacted with the corresponding isothiocyanates under the same condition as described in Example 164 to give the title compounds.

Example 165

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluoro-phenyl)thiocarbamoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.40(s, 1H), 7.35(d, 1H), 7.15(m, 2H), 6.90(m, 3H), 6.77(d, 1H), 6.70(s, 1H), 6.55(d, 1H), 6.42(m, 2H), 5.80(s, 2H), 5.00(s, 2H), 4.70(s, 2H), 3.77(dd, 2H), 2.85(dd, 2H)

LC/MS(MH^+) 557

Example 166

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-N-(4-fluoro-phenyl)thiocarbamoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.50(m, 2H), 7.40(s, 1H), 7.30(t, 1H), 7.15(m, 3H), 7.02(t, 1H), 6.82(s, 1H), 6.70(d, 1H), 6.55(m, 2H), 5.90(s, 2H), 5.10(s, 2H), 4.80(s, 2H), 3.90(dd, 2H), 3.00(dd, 2H)

LC/MS(MH^+) 557

Example 167

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-N-(3-hydroxy-4-methoxyphenyl)thiocarbamoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.47(m, 2H), 7.27(t, 2H), 7.10(d, 1H), 6.87(s, 1H), 6.80(d, 1H), 6.70(m, 3H), 6.80(m, 2H), 5.92(s, 2H), 5.12(s, 2H), 4.80(s, 2H), 3.95(dd, 2H), 3.87(s, 3H), 3.00(dd, 2H)

LC/MS(MH^+) 585

Example 168

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-N-(4-methyl-phenyl)thiocarbamoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.50(d, 1H), 7.47(s, 1H), 7.30(m, 2H), 7.10(q, 5H), 6.85(s, 1H), 6.70(d, 1H), 6.70(m, 2H), 5.90(s, 2H), 5.17(s, 2H), 4.80(s, 2H), 3.98(dd, 2H), 3.05(dd, 2H), 2.35(s, 3H)

LC/MS(MH^+) 553

Example 169

N-{2-[1-(3,4-Methylenedioxyphenylmethyl)-1H-imidazol-5-yl]}ethyl-N-phenylthio-carbamoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.50(d, 1H), 7.47(s, 1H), 7.10-7.40(m, 8H), 6.85(s, 1H), 6.70(d, 1H), 6.70(m, 2H), 5.90(s, 2H), 5.17(s, 2H), 4.80(s, 2H), 3.98(dd, 2H), 3.05(dd, 2H)

LC/MS(MH^+) 539

Example 170

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methylphenyl)thio-carbamoyl-butylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-butylamine(12mg, 0.043mmol) prepared from Preparation Example 27 in dichloromethane(1ml) was added a solution of 3-chloro-4-methylphenyl isothiocyanate(0.5M solution in dichloromethane, 86ul, 0.043mmol). After stirring for 2hr at room temperature, the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(12mg).

^{1}H-NMR($CDCl_3$) δ 7.57-7.70(m, 3H), 7.10-7.40(m, 6H), 7.00(d, 1H), 5.50(s, 2H), 3.97(dd, 2H), 3.55(m, 2H), 3.00(dd, 2H), 2.40(s, 3H), 1.40(m, 3H), 1.00(m, 4H)

LC/MS(MH^+) 466

Example 171-172

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-butylamine prepared from Preparation Example 27 was reacted with the corresponding isothiocyanates under the same condition as described in Example 170 to give the title compounds.

Example 171

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2,4-dimethoxyphenyl)-thiocarbamoyl-butylamine

^{1}H-NMR($CDCl_3$) δ 8.00(m, 1H), 7.65(d, 2H), 7.57(s, 1H), 7.00(d, 1H), 6.55(m, 2H), 5.60(s, 2H), 3.97(dd, 2H), 3.87(s, 6H), 3.55(m, 2H), 3.00(dd, 2H), 1.40(m, 3H), 1.00(m, 4H)

LC/MS(MH^+) 478

Example 172

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)t

hio-carbamoyl-butylamine

^{1}H-NMR($CDCl_3$) δ 7.95(m, 1H), 7.65(d, 3H), 7.57(s, 1H), 7.20(m, 3H), 7.00(s, 1H),6.80(d, 1H), 5.52(s, 2H), 3.97(dd+s, 5H), 3.55(m, 2H), 3.00(dd, 2H), 1.40(m, 3H), 1.00(m, 4H)

LC/MS(MH^+) 449

Example 173

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylphenyl)thio-carbamoyl-2-butenylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-butenylamine(12mg, 0.043mmol) prepared from Preparation Example 30 in dichloromethane(1ml) was added a solution of 4-methylphenyl isothiocyanate(0.5M solution in dichloromethane, 86ul, 0.043mmol). After stirring for 4hr at room temperature, the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(6mg).

^{1}H-NMR($CDCl_3$) δ 7.57-7.70(m, 3H), 7.15-7.30(m, 6H), 7.00(m, 2H), 5.57(m, 2H), 3.97(dd, 2H), 3.55(m, 2H), 3.00(dd, 2H), 2.40(s, 3H), 1.80(m, 2H), 1.30(m, 3H)

LC/MS(MH^+) 430

Example 174-175

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-butenylamine prepared from Preparation Example 30 was reacted with the corresponding isothiocyanates under the same condition as described in Example 173 to give the title compounds.

Example 174

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)-thiocarbamoyl-2-butenylamine

^{1}H-NMR($CDCl_3$) δ 7.67(d, 2H), 7.57(s, 1H), 7.17-7.40(m, 4H), 6.90-7.05(m, 4H), 5.57(m, 2H), 3.98(dd, 2H), 3.85(s, 3H), 3.55(m, 2H), 3.00(dd, 2H), 1.80(m, 2H), 1.30(m, 3H)

LC/MS(MH^+) 446

Example 175

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-butenylamine

^{1}H-NMR($CDCl_3$) δ 8.00(m, 1H), 7.67(d, 2H), 7.57(s, 1H), 7.20(d, 2H), 7.05(s, 1H), 6.80(d, 1H), 5.57(d, 2H), 3.98(dd+s, 5H), 3.55(m, 2H), 3.00(dd, 2H), 1.80(m, 2H), 1.30(m, 3H)

LC/MS(MH^+) 447

Example 176

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-fluorophenyl)thio-carbamoylcyclohexylmethylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-cyclohexylmethylamine(14 mg, 0.043mmol) prepared from Preparation Example 31 in dichloromethane(1ml) was added a solution of 4-fluorophenyl isothiocyanate(0.5M solution in dichloromethane, 86ul, 0.043mmol). After stirring for 6hr at room temperature, the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(14mg).

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.50(s, 1H), 7.23(m, 3H), 7.00-7.20(m, 4H), 6.95(s, 1H), 5.45(s, 2H), 3.95(dd, 2H), 3.35(d, 2H), 2.92(dd, 2H), 1.80(m, 5H),

1.25(m, 4H), 1.00(m, 2H)
LC/MS(MH^+) 476

Example 177-179

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-cyclohexylmethyl-amine prepared from Preparation Example 31 was reacted with the corresponding isothiocyanates under the same condition as described in Example 176 to give the title compounds.

Example 177
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylphenyl)thio-carbamoyl-cyclohexylmethylamine
^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.50(m, 2H), 7.07-7.24(m, 7H), 6.95(s, 1H), 5.45(s, 2H), 3.95(dd, 2H), 3.35(d, 2H), 2.92(dd, 2H), 2.37(s, 3H), 1.80(m, 5H), 1.25(m, 4H), 1.00(m, 2H)
LC/MS(MH^+) 472

Example 178
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-trifluoromethyl-phenyl)thiocarbamoyl-cyclohexylmethylamine
^{1}H-NMR($CDCl_3$) δ 7.50-7.65(m, 7H), 7.40(s, 1H), 7.15(d, 2H), 6.95(s, 1H), 5.45(s, 2H), 3.95(dd, 2H), 3.40(d, 2H), 2.92(dd, 2H), 2.37(s, 3H), 1.80(m, 5H), 1.25(m, 4H), 1.00(m, 2H)
LC/MS(MH^+) 526

Example 179
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-phenylethyl)thio-carbamoyl-cyclohexylmethylamine
^{1}H-NMR($CDCl_3$) δ 7.65(d, 2H), 7.55(s, 1H), 7.15-7.40(m, 7H), 6.95(s, 1H),

5.50(s, 2H), 5.30(t, 1H), 3.95(q, 2H), 3.82(dd, 2H), 2.97(t, 4H), 2.82(dd, 2H), 1.70(m, 3H), 1.50(m, 2H), 1.25(m, 2H), 1.10(m, 2H), 0.70(m, 2H)
LC/MS(MH^+) 486

Example 180
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)thiocarbamoyl-isobutylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-isobutylamine(12mg, 0.043mmol)prepared from Preparation Example 28 in dichloromethane(1ml) was added a solution of 3-chlorophenyl isothiocyanate(0.5M solution in dichloromethane, 86ul, 0.043mmol). The mixture was stirred for 3hr at room temperature. The reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(13mg).
^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.42(s, 1H), 7.10-7.30(m, 7H), 6.95(s, 1H), 5.47(s, 2H), 3.95(dd, 2H), 3.37(d, 2H), 2.95(dd, 2H), 2.10(m, 1H), 1.05(d, 6H)
LC/MS(MH^+) 452

Example 181
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-phenylethyl)thiocarbamoyl-isobutylamine

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-isobutylamine prepared from Preparation Example 28 was reacted with phenethyl isothiocyanate under the same condition as described in Example 180 to give the title compound.
^{1}H-NMR($CDCl_3$) δ 7.61(d, 2H), 7.50(s, 1H), 7.10-7.40(m, 6H), 6.95(s, 1H), 5.47(s, 2H), 3.77-3.98(m, 4H), 2.95(t, 4H), 2.80(dd, 2H), 1.80(m, 1H), 0.75(d,

6H)

LC/MS(MH^+) 446

Example 182

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-chlorophenyl)thio-carbamoylpropylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-propylamine(12mg, 0.044mmol)prepared from Preparation Example 32 in dichloromethane(1ml) was added a solution of 4-chlorophenyl isothiocyanate(0.5M solution in dichloromethane, 86ul, 0.043mmol). After stirring for 3hr at room temperature, the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(12mg).

^{1}H-NMR($CDCl_3$) δ 7.62(dd, 2H), 7.55(s, 1H), 7.10-7.40(m, 7H), 6.97(m, 1H), 5.50(m, 2H), 3.97(dd, 2H), 3.37(m, 1H), 2.95(dd, 2H), 2.15(m, 1H), 1.00(m, 5H)

LC/MS(MH^+) 438

Example 183-184

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-propylamine prepared from Preparation Example 32 was reacted with the corresponding isothiocyanates under the same condition as described in Example 182 to give the title compounds.

Example 183

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methylphenyl)thio-carbamoyl-propylamine

^{1}H-NMR($CDCl_3$) δ 7.50-7.70(m, 8H), 7.15(m, 2H), 6.97(s, 1H), 5.50(m, 2H), 3.97(dd, 2H), 3.37(m, 1H), 2.95(dd, 2H), 2.15(m, 1H), 1.00(m, 5H)
LC/MS(MH^+) 472

Example 184
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-trifluoromethyl-phenyl)thiocarbamoyl-propylamine
^{1}H-NMR($CDCl_3$) δ 7.65(d, 2H), 7.55(s, 1H), 7.10-7.40(m, 7H), 6.97(s, 1H), 5.50(m, 2H), 3.97(dd, 2H), 3.37(m, 1H), 2.95(dd, 2H), 2.15(m, 1H), 1.00(m, 5H)
LC/MS(MH^+) 488

Example 185
N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)thio-carbamoylpentylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-pentylamine(13mg, 0.043mmol) prepared from Preparation Example 29 in dichloromethane(1ml) was added a solution of 3-chlorophenyl isothiocyanate(0.5M solution in dichloromethane, 86ul, 0.043mmol). After stirring for 1hr at room temperature, the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(13mg).
^{1}H-NMR($CDCl_3$) δ 7.65(d, 2H), 7.55(s, 1H), 7.10-7.40(m, 7H), 6.97(s, 1H), 5.50(s, 2H), 3.95(dd, 2H), 3.50(t, 2H), 2.95(dd, 2H), 1.40(m, 4H), 0.95(m, 5H)
LC/MS(MH^+) 466

Example 186
N-{2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)thio-carb

amoyl-2-trifluoromethylbenzylamine

To a solution of N-{2-[1-(4-nitrobenzyl)-1H-imidazol-5-yl]}ethyl-2-trifluoromethylbenzylamine(12mg, 0.03mmol) prepared from Preparation Example 33 in dichloromethane(1ml) was added a solution of 3-chlorophenyl isothiocyanate(0.5M solution in dichloromethane, 60ul, 0.03mmol). After stirring for 2hr at room temperature, the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(15mg).

^{1}H-NMR($CDCl_3$) δ 8.18(d, 2H), 7.80(d, 1H), 7.65(t, 1H), 7.50(m, 2H), 7.32(t, 2H), 7.20(m, 5H), 7.08(d, 1H), 6.92(s, 1H), 5.50(s, 2H), 5.00(s, 2H), 4.00(dd, 2H), 3.00(dd, 2H)

LC/MS(MH^+) 574

Example 187-188

N-{2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]}ethyl-2-trifluoromethyl-benzyl-amine prepared from Preparation Example 33 was reacted with the corresponding isothiocyanates under the same condition as described in Example 186 to give the title compounds.

Example 187

N-{2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 8.18(d, 2H), 7.78(d, 1H), 7.62(t, 1H), 7.50(m, 2H), 7.35(d, 1H), 7.20(d, 2H), 7.08(d, 3H), 6.80(t, 3H), 5.50(s, 2H), 5.00(s, 2H), 4.01(dd, 2H), 3.80(s, 3H), 3.01(dd, 2H)

LC/MS(MH^+) 570

Example 188

N-{2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 8.18(d, 2H), 7.82(d, 1H), 7.78(d, 1H), 7.62(t, 1H), 7.50(m, 3H), 7.35(d, 2H), 7.20(d, 2H), 6.90(s, 1H), 6.72(d, 1H), 5.50(s, 2H), 5.00(s, 2H), 4.01(dd, 2H), 3.90(s, 3H), 3.01(dd, 2H)

LC/MS(MH^+) 571

Example 189

N-{2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methyl-phenyl)thiocarbamoyl-2,3-dichlorobenzylamine

To a solution of N-{2-[1-(4-nitrobenzyl)-1H-imidazol-5-yl]}ethyl-2,3-dichlorobenzylamine(12 mg, 0.03mmol) prepared from Preparation Example 34 in dichloromethane(1ml) was added a solution of 3-chloro-4-methylphenyl isothiocyanate(0.5M solution in dichloromethane, 60ul, 0.03mmol). The mixture was stirred for 2hr at room temperature. And the mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(17mg).

^{1}H-NMR($CDCl_3$) δ 8.20(d, 2H), 7.55(m, 3H), 7.35(t, 1H), 7.22(d, 4H), 7.00-7.15(m, 2H), 6.91(s, 1H), 5.55(s, 2H), 4.95(s, 2H), 4.00(dd, 2H), 3.03(dd, 2H), 2.40(s, 3H)

LC/MS(MH^+) 588

Example 190-194

N-{2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]}ethyl-2,3-dichlorobenzyl-amine prepared from Preparation Example 34 was reacted with the corresponding isothiocyanates under the same condition as described in

Example 189 to give the title compounds.

Example 190

N-{2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)thio-carb amoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 8.20(d, 2H), 7.60(m, 1H), 7.52(s, 1H), 7.35(m, 2H), 7.22(m, 5H), 7.15(t, 2H), 6.91(s, 1H), 5.55(s, 2H), 4.90(s, 2H), 4.00(dd, 2H), 3.03(dd, 2H)

LC/MS(MH^+) 574

Example 191

N-{2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-chlorophenyl)thio-carb amoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 8.20(d, 2H), 7.55(m, 3H), 7.35(m, 3H), 7.10-7.25(m, 5H), 6.91(s, 1H), 5.55(s, 2H), 4.90(s, 2H), 4.00(dd, 2H), 3.03(dd, 2H)

LC/MS(MH^+) 574

Example 192

N-{2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-fluorophenyl)thio-carb amoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 8.20(d, 2H), 7.55(s, 3H), 7.20-7.40(m, 4H), 7.10(m, 2H), 6.95(d, 2H), 6.91(s, 1H), 5.55(s, 2H), 4.90(s, 2H), 4.00(dd, 2H), 3.03(dd, 2H)

LC/MS(MH^+) 558

Example 193

N-{2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 8.20(d, 2H), 7.55(d+s, 2H), 7.20-7.35(m, 4H), 7.20(d, 2H), 7.12(m, 3H), 6.91(m, 3H), 5.55(s, 2H), 4.90(s, 2H), 4.00(dd, 2H), 3.80(s, 3H), 3.03(dd, 2H)

LC/MS(MH^+) 570

Example 194

N-{2-[1-(4-Nitrobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)-thio-carbamoyl-2,3-dichlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 8.20(d, 2H), 7.85(d, 1H), 7.70(s, 1H), 7.55(m, 2H), 7.48(s, 1H), 7.35(t, 1H), 7.22(d, 2H), 7.12(d, 1H), 6.85(s, 1H), 6.76(d, 1H), 5.55(s, 2H), 4.90(s, 2H), 4.03(dd, 2H), 3.90(s, 3H), 3.03(dd, 2H)

LC/MS(MH^+) 571

Example 195

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-(α -methyl-3-chloro)benzylamine

To a solution of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(α -methyl-3-chloro)benzylamine(10mg, 0.027mmol) prepared from Preparation Example 35 in dichloromethane(1ml) was added a solution of 4-methoxyphenyl isothiocyanate(0.5M solution in dichloromethane, 54ul, 0.027mmol). After stirring for 6hr at room temperature, the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(13mg, 91%).

^{1}H-NMR($CDCl_3$) δ 6.81-7.60(m, 14H), 5.84(dd, 1H), 5.28(s, 2H), 3.80(s, 3H), 3.67(m, 2H), 2.76(m, 2H), 1.66(d, 3H)

LC/MS(MH^+) 530

Example 196-197

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(α -methyl-3-chloro)benzylamine prepared from Preparation Example 35 was reacted with the corresponding isothiocyanates under the same condition as

described in Example 195 to give the title compounds.

Example 196

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)-thiocarbamoyl-(α -methyl-3-chloro)benzylamine

H-NMR($CDCl_3$) δ 6.71-7.88(m, 13H), 5.82(dd, 1H), 5.28(s, 2H), 3.91(s, 3H), 3.79(m, 2H), 2.77(m, 2H), 1.67(d, 3H)

LC/MS(MH^+) 531

Example 197

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-fluorophenyl)thio-carbamoyl(α -methyl-3-chloro)benzylamine

H-NMR($CDCl_3$) δ 6.80-7.60(m, 14H), 5.81(dd, 1H), 5.29(s, 2H), 3.78(m, 2H), 2.77(m, 2H), 1.65(d, 3H)

LC/MS(MH^+) 518

Example 198

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methoxyphenyl)thio-carbamoyl-(α -methyl-3-fluoro)benzylamine

To a solution of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(α -methyl-3-fluoro)benzylamine(10mg, 0.026mmol) prepared from Preparation Example 36 in dichloromethane(1ml) was added a solution of 4-methoxyphenyl isothiocyanate(0.5M solution in dichloromethane, 54ul, 0.027mmol). After stirring for 6hr at room temperature, the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(10mg).

^{1}H-NMR($CDCl_3$) δ 6.81-7.60(m, 14H), 5.79(dd, 1H), 5.31(s, 2H), 3.80(s, 3H), 3.74(m, 2H), 2.78(m, 2H), 1.67(d, 3H).

LC/MS(MH^+) 514

Example 199-201

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-(α -methyl-3-fluoro)-benzylamine prepared from Preparation Example 36 was reacted with the corresponding isothiocyanates under the same condition as described in Example 198 to give the title compounds.

Example 199

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-(α -methyl-3-fluoro)benzylamine

^{1}H-NMR($CDCl_3$) δ 6.69-7.73(m, 13H), 5.79(dd, 1H), 5.33(s, 2H), 3.92(s, 3H), 3.81(m, 2H), 2.79(m, 2H), 1.68(d, 3H)

LC/MS(MH^+) 515

Example 200

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-chlorophenyl)thio-carbamoyl(α -methyl-3-fluoro)benzylamine

^{1}H-NMR($CDCl_3$) δ 6.81-7.58(m, 14H), 5.77(dd, 1H), 5.28(s, 2H), 3.79(m, 2H), 2.79(m, 2H), 1.65(d, 3H)

LC/MS(MH^+) 518

Example 201

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylphenyl)thio-carbamoyl(α -methyl-3-fluoro)benzylamine

^{1}H-NMR($CDCl_3$) δ 6.79-7.59(m, 14H), 5.80(dd, 1H), 5.34(s, 2H), 3.79(m, 2H), 2.79(m, 2H), 2.35(s, 3H), 1.66(d, 3H)

LC/MS(MH^+) 498

Example 202

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(4-methoxyphenyl)-N'-methyl]thiocarbamoyl-2-trifluoromethylbenzylamine

<Step 1>

N-(4-Methoxyphenyl)-N-methylthiocarbamoyl chloride

A suspension of N-methyl-*p*-anisidine(5.13g, 37.4mmol) and NaH(60%, 1.65g, 41.1mmol) in anhydrous tetrahydrofuran(100ml) was refluxed for 5hr. To the reaction mixture was added dropwise trimethylsilyl chloride(4.06g, 37.4mmol) at room temperature and then the mixture was refluxed for 1hr. The insoluble material was filtered off, and the filtrate was concentrated *in vacuo*. The residue was distillated *in vacuo* to give(4-methoxyphenyl)-methyl-trimethylsilanylamine(5.95g, 76%) as an yellow oil. To a solution of thiophosgen(1.61ml, 21.1mmol) in anhydrous n-hexane(40ml) was added(4-methoxyphenyl)-methyl-trimethylsilanylamine (5.95g, 76%) at -100℃ and the reaction mixture was stirred for 1hr. The insoluble material was filtered off and the filtrate was concentrated *in vacuo* to give the title compound.

R_f=0.5(Ethyl acetate/n-Hexane=1/3, v/v)

<Step 2>

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(4-methoxyphenyl)-N'-methyl]thiocarbamoyl-2-trifluoromethylbenzylamine

A solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-trifluoromethylbenzylamine prepared from Preparation Example 1 and N-(4-methoxyphenyl)-N-methylthiocarbamoyl chloride in dichloromethane was refluxed for 24hr. The reaction mixture was concentrated *in vacuo*, and the residue was purified by silica gel column chromatography to give the title

compound as white yellow.

R_f=0.5(dichloromethane/methanol = 10/1, v/v)

^{1}H-NMR($CDCl_3$) δ 6.76-7.60(m, 14H), 5.08(s, 2H), 4.65(s, 2H), 3.77(s, 3H), 3.65(m, 2H), 3.42(s, 3H), 2.66(m, 2H)

Example 203

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chlorophenyl)thio-carbamoyl-2-methylphenylamine

To a solution of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-methylphenylamine(20mg, 0.063mmol) prepared from Preparation Example 46 in dichloromethane(1ml) was added a solution of 3-chlorophenyl isothiocyanate(0.5M solution in dichloromethane, 126ul). The mixture was heated for 24hr at 35℃. The reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(14.7mg).

^{1}H-NMR($CDCl_3$) δ 7.57-7.66(m, 3H), 7.45-7.48(m, 3H), 7.15-7.42(m, 6H), 6.90(s, 1H), 6.82(s, 1H), 5.54(dd, 2H), 4.59-4.74(m, 1H), 3.63-3.78(m, 1H), 2.96-3.08(m, 2H), 2.28(s, 3H)

LC/MS(MH^+) 486

Example 204-205

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-2-methylphenyl-amine prepared from Preparation Example 46 was reacted with the corresponding isothiocyanates under the same condition as described in Example 203 to give the title compounds.

Example 204

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-chlorophenyl)thiocarbamoyl-2-methylphenylamine

^{1}H-NMR($CDCl_3$) δ 7.57-7.65(m, 3H), 7.39-7.49(m, 3H), 7.15-7.37(m, 6H), 6.90(s, 1H), 6.79(s, 1H), 5.54(dd, 2H), 4.59-4.74(m, 1H), 3.63-3.78(m, 1H), 2.96-3.07(m, 2H), 2.28(s, 3H)

LC/MS(MH^+) 486

Example 205

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(4-methylphenyl)thio-carbamoyl-2-methylphenylamine

^{1}H-NMR($CDCl_3$) δ 7.59-7.65(m, 4H), 7.36-7.46(m, 3H), 7.16-7.28(m, 6H), 6.91(s, 1H), 6.76(s, 1H), 5.56(dd, 2H), 4.59-4.74(m, 1H), 3.65-3.80(m, 1H), 2.98-3.09(m, 2H), 2.36(s, 3H), 2.30(s, 3H)

LC/MS(MH^+) 466

Example 206

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-chloro-4-methyl-phenyl)thiocarbamoyl-2-trifluoromethylbenzylamine

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-2-trifluoromethylbenzylamine(264mg, 0.66mmol) prepared from Preparation Example 37 in dichloromethane(10ml) was added 3-chloro-4-methylphenyl isothiocyanate(110mg, 0.66mmol) in dichloromethane. After stirring for 1hr at room temperature, the solution was concentrated *in vacuo*. The residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(364mg, 95%).

^{1}H-NMR($CDCl_3$) δ 6.83-7.76(m, 13H), 5.17(s, 2H), 5.03(s, 2H), 3.85(t, 2H), 2.42(t, 2H), 2.13(s, 3H), 2.06(m, 2H)

LC/MS(MH^+) 582

Example 207-241

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-2-trifluoromethyl-benzylamine prepared from Preparation Example 37 was reacted with the corresponding isothiocyanates under the same condition as described in Example 206 to give the title compounds.

Example 207

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-chlorophenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 6.83-7.76(m, 14H), 5.17(s, 2H), 5.03(s, 2H), 3.85(t, 2H), 2.42(t, 2H), 2.06(m, 2H)

LC/MS(MH^+) 568

Example 208

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-chlorophenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 6.83-7.76(m, 14H), 5.17(s, 2H), 5.03(s, 2H), 3.85(t, 2H), 2.42(t, 2H), 2.06(m, 2H)

LC/MS(MH^+) 568

Example 209

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2,4-dichlorophenyl)-thiocarbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 6.83-7.90(m, 13H), 5.17(s, 2H), 5.03(s, 2H), 3.85(t, 2H), 2.42(t, 2H), 2.06(m, 2H)

LC/MS(MH^+) 602

Example 210

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-fluorophenyl)thio-ca

rbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 6.83-7.76(m, 14H), 5.17(s, 2H), 5.03(s, 2H), 3.85(t, 2H), 2.42(t, 2H), 2.06(m, 2H)

LC/MS(MH^+) 552

Example 211

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-fluorophenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 6.83-7.76(m, 14H), 5.17(s, 2H), 5.03(s, 2H), 3.85(t, 2H), 2.42(t, 2H), 2.06(m, 2H)

LC/MS(MH^+) 552

Example 212

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-hydroxy-4-methoxy-phenyl)thiocarbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 6.70-7.77(m, 13H), 5.20(s, 2H), 5.01(s, 2H), 3.90(t, 2H), 3.87(s, 3H), 2.42(t, 2H), 2.06(m, 2H)

LC/MS(MH^+) 580

Example 213

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-methoxyphenyl)-thiocarbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 6.83-7.76(m, 14H), 5.17(s, 2H), 5.03(s, 2H), 3.85(t, 2H), 3.79(s, 3H), 2.42(t, 2H), 2.06(m, 2H)

LC/MS(MH^+) 564

Example 214

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 6.70-7.81(m, 13H), 5.17(s, 2H), 5.03(s, 2H), 3.88(s, 3H),

3.87(t, 2H), 2.42(t, 2H), 2.06(m, 2H)
LC/MS(MH^+) 565

Example 215
N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methylphenyl)thio-carbamoyl-2-trifluoromethylbenzylamine
^{1}H-NMR($CDCl_3$) δ 6.83-7.76(m, 14H), 5.17(s, 2H), 5.03(s, 2H), 3.85(t, 2H), 2.42(t, 2H), 2.09(m, 2H), 2.04(s, 3H)
LC/MS(MH^+) 548

Example 216
N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-methylphenyl)thio-carbamoyl-2-trifluoromethylbenzylamine
^{1}H-NMR($CDCl_3$) δ 6.83-7.76(m, 14H), 5.17(s, 2H), 5.03(s, 2H), 3.85(t, 2H), 2.42(t, 2H), 2.32(s, 3H), 2.06(m, 2H)
LC/MS(MH^+) 548

Example 217
N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-phenylthiocarbamoyl-2-trifluoromethylbenzylamine
^{1}H-NMR($CDCl_3$) δ 6.83-7.76(m, 15H), 5.17(s, 2H), 5.03(s, 2H), 3.85(t, 2H), 2.42(t, 2H), 2.08(m, 2H)
LC/MS(MH^+) 534

Example 218
N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-trifluoromethyl-phenyl)thiocarbamoyl-2-trifluoromethylbenzylamine
^{1}H-NMR($CDCl_3$) δ 6.83-7.76(m, 14H), 5.17(s, 2H), 5.03(s, 2H), 3.85(t, 2H), 2.42(t, 2H), 2.06(m, 2H)
LC/MS(MH^+) 602

Example 219

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-trifluoromethyl-phenyl)thiocarbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 6.83-7.76(m, 14H), 5.17(s, 2H), 5.03(s, 2H), 3.85(t, 2H), 2.42(t, 2H), 2.06(m, 2H)

LC/MS(MH^+) 602

Example 220

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-acetylphenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 576

Example 221

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-benzyloxyphenyl)-thiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 640

Example 222

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-bromophenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 612

Example 223

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-bromophenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.75-7.35(m, 9H), 7.1(m, 5H), 6.85(s, 1H), 5.15(s, 1H), 5.05(s, 1H), 3.85(t, 2H), 2.4(t, 2H), 2.1(m, 2H)

LC/MS(MH^+) 612

Example 224

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-chloro-6-methoxy-phenyl)thiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 598

Example 225

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-nitro-4-chloro-phenyl)thiocarbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR(CDCl3) δ 7.90-7.40(m, 11H), 7.10(dd, 2H), 6.80(s, 1H), 5.15(s, 2H), 5.10(s 2H), 3.85(t, 2H), 2.45(t, 2H), 2.05(m, 2H)

LC/MS(MH^+) 612

Example 226

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-cyanophenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 559

Example 227

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(n-pentyl)thio-carbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 528

Example 228

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-N",N"-dimethyl-aminonaphthyl-1-yl)thiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 627

Example 229

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-ethoxycarbonyl-phenyl)thiocarbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 8.00(dd, 2H), 7.80-7.30(m, 10), 7.10(dd, 2H), 6.85(s, 1H), 5.15(s, 2H), 5.05(s, 2H), 4.35(m, 2H), 3.85(t, 2H), 2.45(t, 2H), 2.10(m, 2H) 1.35(t, 3H)

LC/MS(MH^+) 606

Example 230

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-methylthio-phenyl)thiocarbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 580

Example 231

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(naphthyl-1-yl)thiocarbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.85-7.25(m, 17H), 7.05(dd, 2H), 6.85(s, 1H), 5.15(s, 2H), 3.95(t, 2H), 2.45(t, 2H), 2.15(m, 2H)

LC/MS(MH^+) 584

Example 232

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(tetrahydrofuran-2-ylmethyl)-thiocarbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.65-7.15(m, 9H), 6.90(s, 1H), 5.8(m, 1H), 5.15(s, 2H), 4.95(s, 1H), 3.90-3.50(m, 7H), 2.40(t, 2H), 2.00-1.80(m, 6H)

LC/MS(MH^+) 542

Example 233

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-phenylpropyl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.70-7.05(m, 14H), 6.90(s, 1H), 5.25(m, 1H), 5.20(s, 1H), 4.90(s, 1H), 3.75(t, 2H), 3.6(m, 2H), 2.5-2.35(m, 4H), 2.00-1.80(m, 4H)

LC/MS(MH^+) 576

Example 234

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(n-butyl)thio-carbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 514

Example 235

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-cyclohexylthio-carbamoyl-2-trifluoromethylbenzylamine

LC/MS(MH^+) 540

Example 236

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-cyclooctylthio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.70-7.40(m, 8H), 7.25-7.15(m, 2H), 6.90(s, 1H), 5.20(s, 2H), 4.80(s, 2H), 4.50(m, 1H), 3.90(t, 2H), 2.45(t, 2H), 2.05(m, 2H), 1.80(m, 4H), 1.45(m, 10H)

LC/MS(MH^+) 568

Example 237

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-cyclopropylthio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.75-7.40(m, 7H), 7.15(dd, 1H), 6.90(s, 1H), 5.45(s, 1H), 5.20(s, 2H), 4.80(s, 2H), 3.80(t, 2H), 3.00(m, 1H), 2.40(t, 2H), 2.00(m, 2H), 0.80(m, 2H), 0.40(m, 2H)

LC/MS(MH^+) 498

Example 238

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-ethoxycarbonylthio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.70-7.30(m, 8H), 7.15(dd, 2H), 6.90(s, 1H), 5.60(s, 2H), 5.20(s, 2H), 4.90(s, 2H), 3.85(t, 2H), 2.25(t, 2H), 2.00(m, 2H), 1.70(t, 3H)
LC/MS(MH^+) 530

Example 239
N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-isobutylthiocarbamoyl-2-trifluoromethylbenzylamine
LC/MS(MH^+) 514

Example 240
N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-methoxypropyl)thiocarbamoyl-2-trifluoromethylbenzylamine
^{1}H-NMR($CDCl_3$) δ 7.70-7.35(m, 6H), 7.15(dd, 2H), 6.9(s, 1H), 6.65(m, 1H), 5.15(s, 1H), 4.9(s, 1H), 3.70(m, 2H), 3.40(t, 2H), 2.95(s, 3H), 2.40(t, 2H), 2.00(m, 2H), 1.75(m, 2H)
LC/MS(MH^+) 530

Example 241
N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-morpholin-4-yl)-ethyl]thio-carbamoyl-2-trifluoromethylbenzylamine
^{1}H-NMR($CDCl_3$) δ 7.75-7.15(m, 8H), 6.90(s, 1H), 6.30(br, 1H), 5.20(s, 2H), 4.80(s, 2H), 3.90(t, 2H), 3.55(m, 2H), 3.20(m, 4H), 2.25(m, 4H), 2.20(m, 4H), 2.05(m, 2H)
LC/MS(MH^+) 571

Example 242
N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-fluorophenyl)thio-carbamoyl-2,3-dichlorobenzylamine

To a solution of

N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-2,3-dichlorobenzylamine(10mg, 0.025mmol) prepared from Preparation Example 38 in dichloromethane(1ml) was added a solution of 4-fluorophenyl isothiocyanate(0.5M solution in dichloromethane, 50ul, 0.025mmol). After stirring for 2hr at room temperature, the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(13mg, 96%).

^{1}H-NMR($CDCl_3$) δ 7.65(dd, 2H), 7.50(m, 2H), 7.25(m, 2H), 7.20-6.95(m, 7H), 6.85(s, 1H), 5.15(s, 2H), 4.90(s, 2H), 3.90(t, 2H), 2.45(t, 2H), 2.05(m, 2H)

LC/MS(MH^+) 552

Example 243-249

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-2,3-dichloro-benzylamine prepared from Preparation Example 38 was reacted with the corresponding isothiocyanates under the same condition as described in Example 242 to give the title compounds.

Example 243

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-chloro-4-methyl-phenyl)thiocarbamoyl-2,3-dichlorobenzylamine

LC/MS(MH^+) 582

Example 244

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-chlorophenyl)thio-carbamoyl-2,3-dichlorobenzylamine

LC/MS(MH^+) 568

Example 245

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-fluorophenyl)thio-ca

rbamoyl-2,3-dichlorobenzylamine
LC/MS(MH^+) 552

Example 246

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-methoxyphenyl)-thiocarbamoyl-2,3-dichlorobenzylamine
LC/MS(MH^+) 564

Example 247

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-2,3-dichlorobenzylamine
LC/MS(MH^+) 565

Example 248

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-methylphenyl)thio-carbamoyl-2,3-dichlorobenzylamine
^{1}H-NMR($CDCl_3$) δ 7.60(dd, 2H), 7.50(dd, 2H), 7.30-7.00(m, 9H), 6.85(s, 1H), 5.20(s, 2H), 4.90(s, 2H), 3.90(t, 2H), 2.45(t, 2H), 2.35(s, 3H), 2.10(m, 2H)
LC/MS(MH^+) 548

Example 249

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-trifluoromethyl-phenyl)thiocarbamoyl-2,3-dichlorobenzylamine
^{1}H-NMR($CDCl_3$) δ 7.62(dd, 2H), 7.45(m, 7H), 7.25(m, 1H), 7.15(m, 3H), 6.85(s, 1H), 5.15(s, 2H), 4.95(s, 2H), 3.90(t, 2H), 2.45(t, 2H), 2.10(m, 2H)
LC/MS(MH^+) 602

Example 250-256

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-3-chlorobenzyl-a

mine prepared from Preparation Example 39 was reacted with the corresponding isothiocyanates under the same condition as described in Example 242 to give the title compounds.

Example 250

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-chlorophenyl)thio-carbamoyl-3-chlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.60(d+s, 3H), 7.32(s, 2H), 7.02-7.28(m, 9H), 6.91(s, 1H), 5.20(s, 2H), 4.82(s, 2H), 3.85(t, 2H), 2.43(t, 2H), 2.07(m, 2H)

LC/MS(MH^+) 534

Example 251

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-chlorophenyl)thio-carbamoyl-3-chlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.60(dd, 2H), 7.50(s, 1H), 7.35-7.25(m, 5H), 7.10(m, 6H), 6.90(s, 1H), 5.15(s, 2H), 4.85(s, 2H), 3.90(t, 2H), 2.42(t, 2H), 2.05(m, 2H)

LC/MS(MH^+) 534

Example 252

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-methoxyphenyl)-thiocarbamoyl-3-chlorobenzylamine

LC/MS(MH^+) 530

Example 253

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-3-chlorobenzylamine

LC/MS(MH^+) 531

Example 254

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methylphenyl)thio-c

arbamoyl-3-chlorobenzylamine

^{1}H-NMR($CDCl_3$) δ 7.62(dd, 2H), 7.50(s, 1H), 7.35-7.10(m, 10H), 6.90(s, 1H), 6.80(s, 1H), 5.15(s, 2H), 4.82(s, 2H), 3.95(t, 2H), 2.45(t, 2H), 2.05(m, 2H), 2.00(s, 3H)

LC/MS(MH^+) 514

Example 255

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-chloro-4-methyl-phenyl)thiocarbamoyl-3-chlorobenzylamine

LC/MS(MH^+) 548

Example 256

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-fluorophenyl)thio-carbamoyl-3-chlorobenzylamine

LC/MS(MH^+) 518

Example 257-262

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-2-methylbenzyl-amine prepared from Preparation Example 40 was reacted with the corresponding isothiocyanates under the same condition as described in Example 242 to give the title compounds.

Example 257

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-chloro-4-methyl-phenyl)thiocarbamoyl-2-methylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.60(d+s, 3H), 7.28(m, 3H), 7.02-7.20(m, 5H), 6.85-7.00(m, 3H), 5.20(s, 2H), 4.70(s, 2H), 3.95(t, 2H), 2.45(t, 2H), 2.30(d, 6H), 2.07(m, 2H)

LC/MS(MH^+) 528

Example 258

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-fluorophenyl)thio-carbamoyl-2-methylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.60(d, 3H), 7.28(m, 4H), 6.80-7.20(m, 8H), 5.20(s, 2H), 4.70(s, 2H), 3.97(t, 2H), 2.45(t, 2H), 2.30(s, 3H), 2.07(m, 2H)

LC/MS(MH^+) 498

Example 259

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-methylphenyl)thio-carbamoyl-2-methylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.60(d, 3H), 7.24(d, 4H), 7.10(m, 4H), 6.85-7.02(m, 4H), 5.20(s, 2H), 4.67(s, 2H), 3.95(t, 2H), 2.45(t, 2H), 2.30(d, 6H), 2.07(m, 2H)

LC/MS(MH^+) 494

Example 260

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-chlorophenyl)thio-carbamoyl-2-methylbenzylamine

LC/MS(MH^+) 514

Example 261

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-fluorophenyl)thio-carbamoyl-2-methylbenzylamine

LC/MS(MH^+) 498

Example 262

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-2-methylbenzylamine

LC/MS(MH^+) 511

Example 263-266

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-(naphthyl-1-yl)-methyl-amine prepared from Preparation Example 41 was reacted with the corresponding isothiocyanates under the same condition as described in Example 242 to give the title compounds.

Example 263

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-fluorophenyl)thio-carbamoyl-(naphthyl-1-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.90(m, 3H), 7.60-7.45(m, 6H), 7.30-7.00(m, 6H), 6.85(m, 3H), 5.25(s, 2H), 5.15(s, 2H), 3.95(t, 2H), 2.45(t, 2H), 2.10(m, 2H)

LC/MS(MH^+) 534

Example 264

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl(naphthyl-1-yl)methylamine

LC/MS(MH^+) 547

Example 265

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-chloro-4-methyl-phenyl)thiocarbamoyl-(naphthyl-1-yl)methylamine

LC/MS(MH^+) 564

Example 266

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-methoxyphenyl)-thiocarbamoyl-(naphthyl-1-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.82-8.00(m, 3H), 7.45-7.68(m, 6H), 7.24-7.38(m, 2H), 7.02-7.18(m, 5H), 6.80-6.95(m, 2H), 5.28(s, 2H), 5.17(s, 2H), 4.00(t, 2H), 3.80(s, 3H), 2.45(t, 2H), 2.30(d, 6H), 2.10(m, 2H)

LC/MS(MH^+) 546

Example 267

N-{4-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}butyl-N-(4-chlorophenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

To a solution of N-{4-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}butyl-2-trifluoromethylbenzylamine(15mg, 0.036mmol) prepared from Preparation Example 42 in dichloromethane(1ml) was added a solution of 4-chlorophenyl isothiocyanate(0.5M solution in dichloromethane, 100ul, 0.05mmol). After stirring for 2hr at room temperature, the reaction mixture was purified by short silica gel column chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(18.3mg).

^{1}H-NMR($CDCl_3$) δ 7.74(d, 1H), 7.60-7.64(m, 3H), 7.41-7.51(m, 3H), 7.24-7.30(m, 2H), 7.07-7.18(m, 4H), 6.83(s, 1H), 5.13(s, 2H), 5.09(s, 2H), 3.81(t, 2H), 2.43(t, 2H), 1.78-1.86(m, 2H), 1.56-1.63(m, 2H)

LC/MS(MH^+) 582

Example 268-270

N-{4-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}butyl-2-trifluoromethyl-benzylamine prepared from Preparation Example 42 was reacted with the corresponding isothiocyanates under the same condition as described in Example 267 to give the title compounds.

Example 268

N-{4-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}butyl-N-(4-fluorophenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.74(d, 1H), 7.60-7.67(m, 3H), 7.42-7.51(m, 3H),

6.96-7.20(m, 6H), 6.84(s, 1H), 5.14(s, 2H), 5.09(s, 2H), 3.82(t, 2H), 2.43(t, 2H), 1.75-1.86(m, 2H), 1.56-1.67(m, 2H)
LC/MS(MH^+) 566

Example 269
N-{4-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}butyl-N-(4-methoxyphenyl)thio-carbamoyl-2-trifluoromethylbenzylamine
^{1}H-NMR($CDCl_3$) δ 7.71(d, 1H), 7.58-7.65(m, 3H), 7.42-7.46(m, 3H), 7.03-7.10(m, 5H), 6.82-6.86(m, 2H), 5.12(s, 2H), 5.08(s, 2H), 3.83-3.75(m, 5H), 2.41(t, 2H), 1.73-1.88(m, 2H), 1.55-1.65(m, 2H)
LC/MS(MH^+) 578

Example 270
N-{4-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}butyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-2-trifluoromethylbenzylamine
^{1}H-NMR($CDCl_3$) δ 7.83(d, 1H), 7.73(d, 1H), 7.59-7.66(m, 3H), 7.42-7.51(m, 3H), 7.22(s, 1H), 7.09(d, 2H), 6.81(s, 1H), 6.71(d, 1H), 5.13(s, 4H),3.90(s, 3H), 3.82(t, 2H), 2.42(t, 2H), 1.75-1.89(m, 2H), 1.56-1.67(m, 2H)
LC/MS(MH^+) 579

Example 271
N-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]methyl-N-(4-methoxyphenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

To a solution of N-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]methyl-2-trifluoromethylbenzylamine (10mg, 0.027mmol) prepared from Preparation Example 43 in dichloromethane(1ml) was added a solution of 4-methoxyphenyl isothiocyanate(0.5M solution in dichloromethane, 65ul). After stirring for 1hr at room temperature, the reaction mixture was purified by short silica gel column

chromatography(eluent: dichloromethane/methanol=20/1, v/v) to give the title compound(14mg).

^{1}H-NMR($CDCl_3$) δ 7.40-7.80(m, 6H), 7.20(d, 1H), 7.05(m, 3H), 6.85(m, 5H), 5.60(s, 2H), 5.40(s, 2H), 4.55(s, 2H), 3.80(s, 3H)

LC/MS(MH^+) 536

Example 272-273

N-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]methyl-2-trifluoromethyl-benzylamine prepared from Preparation Example 43 was reacted with the corresponding isothiocyanates under the same condition as described in Example 271 to give the title compounds.

Example 272

N-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]methyl-N-(4-nitrophenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 8.10(d, 2H), 7.50-7.70(m, 5H), 7.35(m, 3H), 6.95-7.15(m, 5H), 5.45(s, 2H), 5.20(s, 2H), 4.75(s, 2H)

LC/MS(MH^+) 551

Example 273

N-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]methyl-N-(2-chlorophenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

^{1}H-NMR($CDCl_3$) δ 7.40-7.75(m, 6H), 7.20(m, 3H), 7.05(m, 5H), 6.85(d, 1H), 5.60(s, 2H), 5.40(s, 2H), 4.60(s, 2H)

LC/MS(MH^+) 540

Example 274

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}acetyl-N-(4-methoxyphenyl)thio-carbamoyl-2-trifluoromethylbenzylamine

To a suspension of NaH(24.1mg, 0.6mmol) in dimethylformamide(5ml) was added N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}acetyl-2-trifluoromethylbenzyl-amine (200mg, 0.5mmol) prepared from Preparation Example 44 at -78℃. After stirring for 10minute at the same temperature, 4-methoxyphenyl isothiocyanate(81mg, 0.5mmol) was added to the mixture. The reaction mixture was standed for 24hr at room temperature and extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulfate, concentrated *in vacuo*. The residue was recrystallized with ethanol to give the title compound(109mg, 38%).

R_f=0.4(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.46-7.74(m, 7H), 6.91-7.10(m, 6H), 6.83(s, 1H), 5.06-5.11(m, 4H), 3.87(s, 3H), 3.25(s, 2H)

LC/MS(MH^+) 564

Example 275

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}acetyl-N-(2-methoxypyridin-5-yl)thio-carbamoyl-2-trifluoromethylbenzylamine

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}acetyl-2-trifluoromethyl-benzylamine prepared from Preparation Example 44 was reacted with 2-methoxypyridin-5-yl isothiocyanates under the same condition as described in Example 274 to give the title compound.

R_f=0.4(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 11.52(s, 1H), 7.88(s, 1H), 7.45-7.72(m, 7H), 7.26-7.31(m, 2H), 7.07(d, 2H), 6.82(s, 1H), 5.09(s, 2H), 5.05(d, 2H), 3.98(s, 3H), 3.26(s, 2H)

LC/MS(MH^+) 565

Example 276

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propionyl-N-(4-methoxyphenyl)-thio-carbamoyl-2-trifluoromethylbenzylamine

To a suspension of NaH(60%, 40.1mg, 1.00mmol) in dimethylformamide(8ml) was added N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propionyl-2-trifluoromethylbenzylamine(345mg, 0.84mmol) prepared from Preparation Example 45 at -40℃. To the reaction mixture was added a solution of 4-methoxyphenyl isothiocyanate(136mg, 0.84mmol) in dimethylformamide(1ml) and stirred for 30min at the same temperature. After stirring for 3hr at room temperature, the reaction mixture was extracted with ethyl acetate. The organic layer was washed with water and dried over anhydrous sodium sulfate, concentrated *in vacuo*. The residue was recrystallized with ethanol to give the title compound(115mg, 24%).

^{1}H-NMR($CDCl_3$) δ 7.48-7.66(m, 6H), 7.33-7.37(m, 1H), 7.06(d, 2H), 6.86(d, 2H), 6.68(s, 1H), 5.23(s, 2H), 5.15(s, 2H), 3.76(s, 3H), 2.84(t, 2H), 2.67(t, 2H)
LC/MS(MH^+) 578

Example 277

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(3-chloro-4-methyl-phenyl)-S-methyl]isothiocarbamoyl-2-trifluoromethylbenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methylphenyl)thiocarbamoyl-2-trifluoromethylbenzylamine(173mg, 0.304mmol) prepared from Example 16 in dichloromethane(2ml) was added iodomethane(129mg, 0.912mmol). The mixture was stirred for 24hr at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(64mg, 36%).

R_f=0.3(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.74(d, 1H), 7.50(m, 4H), 7.40(m, 2H), 7.12(d, 1H), 6.90(m, 4H), 6.72(dd, 1H), 5.26(s, 2H), 5.00(s, 2H), 3.52(dd, 2H), 2.92(dd, 2H), 2.40(s, 3H), 1.90(s, 3H)

LC/MS(MH^+) 582

Example 278-281

The compounds prepared from Example 17, Example 1, Example 2, Example 3 were reacted with iodomethane under the same condition as described in Example 277 to give the title compounds.

Example 278

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(benzyl-S-methyl)-isothiocarbamoyl-2-trifluoromethylbenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 548

Example 279

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(4-methoxyphenyl)-S-methyl]isothiocarbamoyl-2-trifluoromethylbenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.88(d, 1H), 7.33-7.72(m, 6H), 7.23(s, 1H), 6.88-7.07(m, 4H), 6.82(s, 1H), 5.26(s, 2H), 4.97(s, 2H), 3.83(s, 3H), 3.45(t, 3H), 2.83(t, 2H), 1.82(s, 3H)

LC/MS(MH^+) 564

Example 280

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-2-trifluoromethylbenzylamine

R_f=0.30(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.72-7.76(m, 2H), 7.43-7.61(m, 5H), 7.19-7.38(m, 3H), 6.96(d, 2H), 6.72(d, 1H), 5.24(s, 2H), 5.02(s, 2H), 3.94(s, 3H), 3.53(t, 3H), 2.79(t, 2H), 1.82(s, 3H)

LC/MS(MH^+) 565

Example 281

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(4-methylphenyl)-S-methyl]isothiocarbamoyl-2-trifluoromethylbenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.68(d, 1H), 7.34-7.68(m, 6H), 7.06(d, 2H), 6.88-6.92(m, 2H), 6.77(d, 2H), 5.23(s, 2H), 4.98(s, 2H), 3.47(t, 3H), 2.82(t, 2H), 2.34(s, 3H),1.82(s, 3H)

LC/MS(MH^+) 548

Example 282

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(3-chloro-4-methyl-phenyl)-S-methyl]isothiocarbamoyl-2,3-dichlorobenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methylphenyl)thiocarbamoyl-2,3-dichlorobenzylamine(24.9mg, 0.048mmol) prepared from Example 47 in dichloromethane(1ml) was added iodomethane(34.1mg, 0.24mmol). The mixture was stirred for 24hr at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(9.8mg, 36%).

R_f=0.3(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 582

Example 283-284

The compounds prepared from Example 55, Example 41 were reacted with iodomethane under the same condition as described in Example 282 to give the title compounds.

Example 283

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(4-fluorophenyl)-S-methyl]isothiocarbamoyl-2,3-dichlorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.41-7.54(m, 3H), 7.19-7.26(m, 2H), 7.01-7.09(m, 2H), 6.90-6.99(m, 4H), 6.76-6.82(m, 2H), 5.25(s, 2H), 4.84(s, 2H), 3.52(t, 2H), 2.81(m, 2H), 1.81(s.3H)

LC/MS(MH^+) 552

Example 284

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(4-methoxyphenyl)-S-methyl]isothiocarbamoyl-2,3-dichlorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.48-7.52(m, 3H), 7.40-7.47(m, 1h), 7.19-7.27(m, 2H), 7.07-7.11(m, 1H), 6.86-6.92(m, 3H), 6.75-6.82(m, 4H), 5.27(s, 2H), 4.85(s, 2H), 3.82(s, 3H), 3.52(t, 2H), 2.82(t, 2H), 1.82(s, 3H)

LC/MS(MH^+) 563

Example 285

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(3-chloro-4-methyl-phenyl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methylphenyl

)thiocarbamoyl-3-chlorobenzylamine(24.9mg, 0.048mmol) prepared from Example 63 in dichloromethane(1ml) was added iodomethane(34.1mg, 0.24mmol). The mixture was stirred for 24hr at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(9.8mg, 36%).

R_f=0.3(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 548

Example 286-288

The compounds prepared from Example 60, Example 66, Example 67 were reacted with iodomethane under the same condition as described in Example 285 to give the title compounds.

Example 286

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(3-fluorophenyl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.52-7.57(m, 2H), 7.13-7.34(m, 5H), 6.92-6.96(m, 3H), 6.57-6.77(m, 4H), 5.24(s, 2H), 4.79(s, 2H), 3.58(t, 2H), 2.78(t, 2H), 1.86(s, 3H)

LC/MS(MH^+) 518

Example 287

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(4-methoxyphenyl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.49-7.53(m, 3H), 7.24-7.35(m, 4H), 7.12-7.16(m, 1H), 6.79-6.96(m, 6H), 5.23(s, 2H), 4.77(s, 2H), 3.82(s, 3H), 3.54(t, 2H), 2.73(t, 2H), 1.85(s, 3H)

LC/MS(MH^+) 530

Example 288

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine

R_f=0.30(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 531

Example 289

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(3-chloro-4-methylphenyl)-S-methyl]isothiocarbamoyl-3-fluorobenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methylphenyl)thiocarbamoyl-3-fluorobenzylamine(38.3mg, 0.27mmol) prepared from Example 76 in dichloromethane(1ml) was added iodomethane(38.3mg, 0.27mmol). The mixture was stirred for 24hr at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(10.9mg, 38%).

R_f=0.3(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 532

Example 290-292

The compounds prepared from Example 77, Example 78, Example 81 were reacted with iodomethane under the same condition as described in Example 289 to give the title compounds.

Example 290

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(3-chlorophenyl)-S-methyl]isothiocarbamoyl-3-fluorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.49-7.56(m, 3H), 7.17-7.33(m, 3H), 6.92-7.01(m, 3H), 6.74-6.89(m, 5H), 5.24(s, 2H), 4.78(s, 2H), 3.52(t, 2H), 2.71(t, 2H), 1.83(s, 3H)

LC/MS(MH^+) 518

Example 291

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(4-methoxyphenyl)-S-methyl]isothiocarbamoyl-3-fluorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.51-7.54(m, 3H), 7.16-7.19(m, 2H), 6.79-7.05(m, 9H), 5.26(s, 2H), 4.77(s, 2H), 3.83(s, 3H), 3.53(t, 2H), 2.74(t, 2H), 1.82(s, 3H)

LC/MS(MH^+) 514

Example 292

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(3-trifluoromethyl-phenyl)-S-methyl]isothiocarbamoyl-3-fluorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 552

Example 293

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(3-chloro-4-methyl-phenyl)-S-methyl]isothiocarbamoyl-2,3-difluorobenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methylphenyl)thiocarbamoyl-2,3-difluorobenzylamine(28.0mg, 0.052mmol) prepared from Example 47 in dichloromethane(1ml) was added iodomethane(36.9mg, 0.26mmol). The mixture was stirred for 24hr at room temperature. The reaction

mixture was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(9.15mg, 32%).

R_f=0.3(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 550

Example 294-297

The compounds prepared from Example 94, Example 92, Example 96, Example 97 were reacted with iodomethane under the same condition as described in Example 293 to give the title compounds.

Example 294

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(3-chlorophenyl)-S-methyl]-isothiocarbamoyl-2,3-difluorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.48-7.58(m, 3H), 6.72-7.23(m, 10H), 5.24(s, 2H), 4.83(s, 2H), 3.53(t, 2H), 2.76(t, 2H), 1.86(s, 3H)

LC/MS(MH^+) 536

Example 295

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(3-fluorophenyl)-S-methyl]isothiocarbamoyl-2,3-difluorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.50-7.57(m, 3H), 6.92-7.22(m, 6H), 6.52-6.75(m, 4H), 5.23(s, 2H), 4.84(s, 2H), 3.53(t, 2H), 2.77(t, 2H), 1.86(s, 3H)

LC/MS(MH^+) 520

Example 296

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(4-methoxyphenyl)-S-m

ethyl]isothiocarbamoyl-2,3-difluorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 532

Example 297

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-2,3-difluorobenzylamine

R_f=0.30(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.68(d, 1H), 7.55(d, 2H), 7.50(s, 1H), 6.92-7.18(m, 7H), 6.68(d, 1H), 5.21(s, 2H), 4.83(s, 2H), 3.96(s, 3H), 3.56(t, 2H), 2.76(t, 2H), 1.84(s, 3H)

LC/MS(MH^+) 533

Example 298

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(3-chloro-4-methyl-phenyl)-S-methyl]isothiocarbamoyl-4-trifluoromethylbenzylamine

To a solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(3-chloro-4-methylphenyl)thiocarbamoyl-4-trifluoromethylbenzylamine(27.8mg, 0.049mmol) prepared from Example 105 in dichloromethane(1ml) was added iodomethane(34.8mg, 0.25mmol). The mixture was stirred for 24hr at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(10.5mg, 37%).

R_f=0.3(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 582

Example 299-301

The compounds prepared from Example 109, Example 103, Example 107 were reacted with iodomethane under the same condition as described in Example 298 to give the title compounds.

Example 299

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(3-fluorophenyl)-S-methyl]isothiocarbamoyl-4-trifluoromethylbenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.62(d, 2H), 7.50-7.58(m, 3H), 7.37(d, 2H), 7.17-7.28(m, 2H), 6.88-7.83(m, 2H), 6.54-6.73(m, 3H), 5.21(s, 2H), 4.83(s, 2H), 3.52(t, 2H), 2.74(t, 2H), 1.86(s, 3H)

LC/MS(MH^+) 552

Example 300

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(4-fluorophenyl)-S-methyl]isothiocarbamoyl-4-trifluoromethylbenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 552

Example 301

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(4-methoxyphenyl)-S-methyl]isothiocarbamoyl-4-trifluoromethylbenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.51-7.53(m, 3H), 7.38(d, 2H), 6.79-7.92(m, 7H), 5.23(s, 2H), 4.82(s, 2H), 3.83(s, 3H), 3.55(t, 2H), 2.75(t, 2H), 1.86(s, 3H)

LC/MS(MH^+) 564

Example 302

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(2-methoxypyridin-5-yl)-S-methyl]thiocarbamoyl-(naphthyl-1-yl)methylamine

To a solution of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-(naphthyl-1-yl)methylamine(27.0mg, 0.051mmol) prepared from Example 108 in dichloromethane(1ml) was added iodomethane(36.0mg, 0.25mmol). The mixture was stirred for 24hr at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(10.0mg, 36%).

R_f=0.3(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.85(m, 2H), 7.76(m, 2H), 7.50(m, 2H), 7.40(m, 4H), 7.20(m, 2H), 6.75(m, 4H), 5.20(s, 2H), 5.06(s, 2H), 3.90(s, 3H), 3.50(dd, 2H), 2.60(dd, 2H), 1.82(s, 3H)

LC/MS(MH^+) 547

Example 303

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]thiocarbamoyl-2-trifluoromethylbenzylamine

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine(150mg, 0.27mmol) prepared from Example 214 in dichloromethane(1ml) was added iodomethane(156mg, 1.10mmol). The mixture was stirred for 24hr at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(60mg, 38%).

R_f=0.3(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.75(d, 1H), 7.60(m, 4H), 7.48(s, 1H), 7.38(t, 3H), 7.22(dd, 1H), 7.05(d, 2H), 6.87(s, 1H), 6.67(d, 1H), 5.12(s, 2H), 4.98(s, 2H),

3.90(s, 3H), 3.45(t, 2H), 2.35(t, 2H), 1.95(m, 2H), 1.86(s, 3H)
LC/MS(MH^+) 579

Example 304-306

The compounds prepared from Example 213, Example 207, Example 210 were reacted with iodomethane under the same condition as described in Example 303 to give the title compounds.

Example 304
N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(4-methoxyphenyl)-S-methyl]isothiocarbamoyl-2-trifluoromethylbenzylamine
R_f=0.35(dichloromethane/methanol=20/1, v/v)
^{1}H-NMR($CDCl_3$) δ 7.32-7.70(m, 6H), 7.04(d, 2H), 6.85(m, 5H), 5.12(s, 2H), 4.98(s, 2H), 3.80(s, 3H), 3.45(t, 2H), 2.35(t, 2H), 1.95(m, 2H), 1.86(s, 3H)
LC/MS(MH^+) 578

Example 305
N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(3-chlorophenyl)-S-methyl]isothiocarbamoyl-2-trifluoromethylbenzylamine
R_f=0.35(dichloromethane/methanol=20/1, v/v)
^{1}H-NMR($CDCl_3$) δ 7,51-7.64(m, 4H), 7.28-7.45(m, 3H), 7.14-7.23(m, 1H), 7.04(d, 2H), 6.80-6.96(m, 4H), 5.13(s, 2H), 4.96(s, 2H), 3.43(t, 2H), 2.14(t, 2H), 1.95-2.03(m, 2H), 1.84(s, 3H)
LC/MS(MH^+) 582

Example 306
N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(3-fluorophenyl)-S-methyl]isothiocarbamoyl-2-trifluoromethylbenzylamine
R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7,50-7.68(m, 4H), 7.36-7.42(m, 3H), 7.16-7.24(m, 1H), 7.03(d, 2H), 6.84(s, 1H), 6.62-6.73(m, 3H), 5.08(s, 2H), 4.94(s, 2H), 3.46(t, 2H), 2.16(t, 2H), 1.93-1.97(m, 2H), 1.87(s, 3H)

LC/MS(MH^+) 566

Example 307

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(3-chloro-4-methylphenyl)-S-methyl]isothiocarbamoyl-2,3-dichlorobenzylamine

To a solution of N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-chloro-4-methylphenyl)thiocarbamoyl-2,3-dichlorobenzylamine(26.5mg, 0.046mmol) prepared from Example 243 in dichloromethane(1ml) was added iodomethane(32.6mg, 0.230mmol). The mixture was stirred for 24hr at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(8.5mg, 31%).

R_f=0.3(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 596

Example 308-311

The compounds prepared from Example 244, Example 245, Example 247 were reacted with iodomethane under the same condition as described in Example 307 to give the title compounds.

Example 308

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(3-chlorophenyl)-S-methyl]isothiocarbamoyl-2,3-dichlorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.62(d, 2H), 7.54(s, 1H), 7.08-7.28(m, 6H), 6.90-6.97(m, 2H), 6.89(dd, 1H), 5.15(s, 2H), 4.92(s, 2H), 3.49(t, 2H), 2.16(t, 2H), 1.90-1.97(m, 2H), 1.84(s, 3H)

LC/MS(MH^+) 582

Example 309

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(3-fluorophenyl)-S-methyl]isothiocarbamoyl-2,3-dichlorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 566

Example 310

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(4-methoxyphenyl)-S-methyl]isothiocarbamoyl-2,3-dichlorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.62(d, 2H), 7.57(s, 1H), 7.44(d, 1H), 7.06-7.13(m, 4H), 6.83-6.95(m, 5H), 5.13(s, 2H), 4.92(s, 2H), 3.79(s, 3H),3.47(t, 2H), 2.17(t, 2H), 1.91-1.98(m, 2H), 1.84(s, 3H)

LC/MS(MH^+) 578

Example 311

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-2,3-dichlorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.71(s, 1H), 7.73(d, 2H), 7.57(s, 1H), 7.42(d, 1H), 7.06-7.30(m, 5H), 6.95(s, 1H), 6.68(dd, 1H), 5.14(s, 2H), 4.92(s, 2H), 3.91(s, 3H), 3.52(t, 2H), 2.18(t, 2H), 1.91-1.98(m, 2H), 1.83(s, 3H)

LC/MS(MH^+) 579

Example 312

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(3-chloro-4-methylphenyl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-chloro-4-methylphenyl)thiocarbamoyl-3-chlorobenzylamine(27.2mg, 0.049mmol) prepared from Example 255 in dichloromethane(1ml) was added iodomethane(35.1mg, 0.248mmol). The mixture was stirred for 24hr at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(10.6mg, 38%).

R_f=0.3(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 562

Example 313-317

The compounds prepared from Example 250, Example 251, Example 256, Example 252, Example 253 were reacted with iodomethane under the same condition as described in Example 312 to give the title compounds.

Example 313

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(3-chlorophenyl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.62(d, 2H), 7.54(d, 2H), 7.23-7.32(m, 3H), 7.03-7.18(m, 4H), 6.76-6.95(m, 4H), 5.08(s, 2H), 4.69(s, 2H), 3.44(t, 2H), 2.09(t, 2H), 1.83(s, 3H), 1.81-1.87(m, 2H)

LC/MS(MH^+) 548

Example 314

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(4-chlorophenyl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 548

Example 315

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(3-fluorophenyl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.62(d, 2H), 7.53(d, 2H), 7.24-7.30(m, 3H), 7.03-7.21(m, 4H), 6.96(s, 1H), 6.59-6.70(m, 3H), 5.07(s, 2H), 4.71(s, 2H), 3.43(t, 2H), 2.23(t, 2H), 1.83(s, 3H), 1.81-1.86(m, 2H)

LC/MS(MH^+) 532

Example 316

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(4-methoxyphenyl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.61(d, 2H), 7.52(d, 2H), 7.26-7.31(m, 3H), 7.10-7.16(m, 1H), 7.07(d, 2H), 6.83-6.91(m, 5H), 5.06(s, 2H), 4.70(s, 2H), 3.79(s, 3H), 3.43(t, 2H), 2.30(t, 2H), 1.83(s, 3H), 1.78-1.81(m, 2H)

LC/MS(MH^+) 544

Example 317

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.75(d, 1H), 7.62(d, 2H), 7.50(s, 1H), 7.19-7.29(m, 4H), 7.06-7.15(m, 3H), 6.90(s, 1H), 6.69(d, 1H), 5.10(s, 2H), 4.73(s, 2H), 3.93(s, 3H), 3.49(t, 2H), 2.34(t, 2H), 1.94(s, 3H), 1.62-1.90(m, 2H)

LC/MS(MH^+) 545

Example 318

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(3-chloro-4-methylphenyl)-S-methyl]isothiocarbamoyl-2-methylbenzylamine

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-chloro-4-methylphenyl)thiocarbamoyl-2-methylbenzylamine(29.1mg, 0.055mmol) prepared from Example 257 in dichloromethane(1ml) was added iodomethane(39mg, 0.275mmol). The mixture was stirred for 24hr at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(9.5mg, 32%).

R_f=0.3(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 542

Example 319-321

The compounds prepared from Example 260, Example 261, Example 262 were reacted with iodomethane under the same condition as described in Example 318 to give the title compounds.

Example 319

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(3-chlorophenyl)-S-methyl]isothiocarbamoyl-2-methylbenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.62(d, 2H), 7.53(s, 1H), 7.04-7.31(m, 7H), 6.91-6.95(m, 4H), 5.10(s, 2H), 4.74(s, 2H), 3.43(t, 2H), 2.24-2.33(m, 5H), 1.86(s, 3H), 1.81-1.85(m, 2H)

LC/MS(MH^+) 528

Example 320

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(3-fluorophenyl)-S-methyl]isothiocarbamoyl-2-methylbenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.62(d, 2H), 7.52(s, 1H), 7.05-7.23(m, 7H), 6.88(s, 1H), 6.62-6.72(m, 3H), 5.08(s, 2H), 4.72(s, 2H), 3.42(t, 2H), 2.25-2.31(m, 5H), 1.88(s, 3H), 1.82-1.87(m, 2H)

LC/MS(MH^+) 512

Example 321

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-2-methylbenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 525

Example 322

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(4-methoxyphenyl)-S-methyl]isothiocarbamoyl-2-methylbenzylamine

<Step 1>

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(4-methoxyphenyl)thio-carbamoyl-2-methylbenzylamine

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-2-methylbenzylamine prepared from Preparation Example 40 was reacted with 4-methoxyphenyl isothiocyanate under the same condition as described in Example 242 to give the title compound.

<Step 2>

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(4-methoxyphenyl)-S-methyl]isothiocarbamoyl-2-methylbenzylamine

The compound prepared from <Step 1> was reacted with iodomethane under the same condition as described in Example 318 to give the title compound.

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.60(d, 2H), 7.52(s, 1H), 7.12-7.22(m, 4H), 7.05(d, 2H), 6.85-6.91(m, 5H), 5.06(s, 2H), 4.73(s, 2H), 3.79(s, 3H), 3.43(t, 2H), 2.26-2.33(m, 5H), 1.80-1.87(m, 5H)

LC/MS(MH^+) 524

Example 323

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(3-chloro-4-methylphenyl)-S-methyl]isothiocarbamoyl-(naphthyl-1-yl)methylamine

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(3-chloro-4-methylphenyl)thiocarbamoyl-(naphthyl-1-yl)methylamine(30mg, 0.053mmol) prepared from Example 265 in dichloromethane(1ml) was added iodomethane(60mg, 0.43mmol). The mixture was stirred for 24hr at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(11mg, 37%).

R_f=0.3(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 578

Example 324-326

The compounds prepared from Example 263, Example 266, Example 264 were reacted with iodomethane under the same condition as described in Example 323 to give the title compounds.

Example 324

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(3-fluorophenyl)-S-methyl]isothiocarbamoyl-(naphthyl-1-yl)methylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

LC/MS(MH^+) 548

Example 325

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(4-methoxyphenyl)-S-methyl]isothiocarbamoyl-(naphthyl-1-yl)methylamine

^{1}H-NMR($CDCl_3$) δ 7.81-8.06(m, 3H), 7.43-7.62(m, 5H), 7.30-7.38(m, 3H), 6.83-7.07(m, 6H), 5.23(s, 2H), 5.03(s, 2H), 3.93(s, 3H), 3.43(t, 2H), 2.24(t, 2H), 1.87(s, 3H), 1.78-1.85(m, 2H)

LC/MS(MH^+) 560

Example 326

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-(naphthyl-1-yl)methylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.81-8.03(m, 3H), 7.42-7.62(m, 6H), 7.28-7.35(m, 3H), 7.03(d, 2H), 6.84(s, 1H), 6.72(d, 1H), 5.22(s, 2H), 5.01(s, 2H), 3.92(s, 3H), 3.46(t, 2H), 2.24(t, 2H), 1.91(s, 3H), 1.781-1.89(m, 2H)

LC/MS(MH^+) 561

Example 327

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(3-chloro-4-methylphenyl)-S-methyl]isothiocarbamoyl-2-trifluoromethylbenzylamine HCl

A solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(3-chloro-4-methylphenyl)-S-methyl]isothiocarbamoyl-2-trifluoromethylbenzylamine(200mg, 0.34mmol) prepared from Example 277 in ethyl acetate(10ml) was bubbled with HCl gas at ice bath for 3 minute. The reaction mixture was poured into diethyl ether(100ml) and the resulting solid was filtered to give the title compound(200mg, 95.1%).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(CD_3OD-d_4) δ 9.12(s, 1H), 7.60-7.90(m, 6H), 7.55(m, 2H), 7.40(q, 4H), 5.65(s, 2H), 5.20(s, 2H), 4.10(dd, 2H), 3.10(dd, 2H), 2.40(s, 3H), 2.20(s, 3H)

Example 328

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-2-trifluoromethylbenzylamine 2HCl

A solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-2-trifluoromethylbenzylamine(1.20g, 2.10mmol) prepared from Example 280 in ethyl acetate(10ml) was bubbled with HCl gas at ice bath for 3 minute. The reaction mixture was poured into diethyl ether(100ml) and the resulting solid was filtered to give the title compound(1.15g).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(CD_3OD-d_4) δ 9.10(s, 1H), 8.25(m, 1H), 8.07(dd, 1H), 7.80(d, 1H), 7.59-7.79(m, 4H), 7.55(d, 1H), 7.40(d, 2H), 7.22(d, 1H), 5.68(s, 2H), 5.20(s, 2H), 4.12(s, 3H), 4.05(dd, 2H), 3.15(dd, 2H), 2.18(s, 3H)

Example 329

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(4-fluorophenyl)-S-met hyl]isothiocarbamoyl-2,3-dichlorobenzylamine HCl

A solution of N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(4-fluorophenyl)-S-met hyl]isothiocarbamoyl-2,3-dichlorobenzylamine(455mg, 0.824mmol) prepared from Example 283 in dichloromethane(30ml) was bubbled with HCl gas at ice bath for 3 minute. The reaction mixture was concentrated *in vacuo* and the residue was recrystallized with dichloromethane to give the title compound(356mg, 75%).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6 + TFA-d) δ 7.76-8.12(m, 3H), 7.62-7.68(m, 2H), 7.41-7.45(m,3H), 7.25-7.39(m, 4H), 5.66(s, 2H), 5.04(s, 2H), 3.91(t, 2H), 3.07(t, 2H), 1.98(s, 3H)

Example 330

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(4-methoxyphenyl)-S-m ethyl]isothiocarbamoyl-2,3-dichlorobenzylamine HCl

A solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(4-methoxyphenyl)-S-m ethyl]isothiocarbamoyl-2,3-dichlorobenzylamine(226mg, 0.400mmol) prepared from Example 284 in dichloromethane(20ml) was bubbled with HCl gas at ice bath for 5 minute. The reaction mixture was concentrated *in vacuo* and the residue was solidified with dichloromethane to give the title compound(216mg, 90%).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6 + TFA-d) δ 9.29(s, 1H), 7.74-7.81(m, 3H), 7.65(d, 1H), 7.38-7.45(m, 4H), 7.03-7.36(m, 2H), 7.00(d, 2H), 5.63(s, 2H), 5.05(s, 2H), 3.92(t, 2H), 3.77(s, 3H), 3.05(t, 2H), 2.03(s, 3H)

Example 331

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-2,3-dichlorobenzylamine 2HCl

<Step 1>

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-2,3-dichlorobenzylamine

The compound prepared from Example 42 was reacted with iodomethane under the same condition as described in Example 282 to give the title compound.

<Step 2>

N-{2-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-2,3-dichlorobenzylamine 2HCl

A solution of N-{2-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}ethyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-2,3-dichlorobenzylamine(325mg, 0.547mmol) prepared from <Step 1> in dichloromethane(25ml) was bubbled with HCl gas at ice bath for 3 minute. The reaction mixture was concentrated *in vacuo* and the residue was washed with dichloromethane. The resulting solid was dissolved in methanol(4ml) and the solution was poured into diethyl ether(100ml). The resulting solid was filtered to give the title compound(304mg, 89%).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6 + TFA-d) δ 9.31(s, 1H), 8.08(d, 1H), 7.71-7.81(m, 3H), 7.63-7.68(m, 2H), 7.32-7.45(m, 4H), 6.94(d, 1H), 5.66(s, 2H), 5.04(s, 2H), 3.88(s, 3H), 3.82-3.87(m, 2H), 3.08(t, 2H), 2.03(s, 3H)

Example 332

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(4-methoxyphenyl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine HCl

A solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(4-methoxyphenyl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine(500mg, 0.919mmol) prepared from Example 316 in dichloromethane(25ml) was bubbled with HCl gas at ice bath for 5 minute. The reaction mixture was concentrated *in vacuo* to give the title compound(532mg, 95%).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 6.98-9.38(m, 14H), 5.65(s, 2H), 5.10(s, 2H), 3.80(m, 2H), 3.75(s, 3H), 2.60(m, 2H), 2.09(s, 3H), 2.01(m, 2H)

Example 333

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine 2HCl

A solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine(500mg, 0.917mmol) prepared from Example 317 in dichloromethane(25ml) was bubbled with HCl gas at ice bath for 5 minute. The reaction mixture was concentrated *in vacuo* to give the title compound(566mg, 98%).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 6.92-9.38(m, 13H), 5.66(s, 2H), 5.17(s, 2H), 3.94(s, 3H), 3.82(m, 2H), 2.60(m, 2H), 2.13(s, 3H), 2.02(m, 2H)

Example 334

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine 2oxalic acid

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine(500mg, 0.92mmol) prepared from Example 317 in ethanol(10ml) was added oxalic acid(230mg, 1.84mmol) and the reaction mixture was stirred for 2hr at room temperature. Diethyl ether(100ml) was added and the resulting solid was filtered to give the title compound(570mg, 85.4%).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 8.60(s, 1H), 7.95(d, 2H), 7.60(s, 1H), 7.10-7.40(m, 8H), 6.75(d, 1H), 5.45(s, 2H), 4.73(s, 2H), 3.80(s, 3H), 3.45(t, 2H), 2.45(t, 2H), 1.95(s, 3H), 1.80(t, 2H)

Example 335

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine 2methanesulfonic acid

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine(500mg, 0.92mmol) prepared from Example 317 in ethanol(10ml) was added methanesulfonic acid(119ul, 1.84mmol) and the reaction mixture was stirred for 2hr at room temperature. Diethyl ether(100ml) was added and the resulting solid was recrystallized with dichloromethane to give the title compound(370mg, 50.9%).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 9.20(s, 1H), 8.05(s, 1H), 7.88(d, 2H), 7.65(m, 2H), 7.40(m, 5H), 7.25(m, 1H), 6.92(d, 1H), 5.60(s, 2H), 5.00(s, 2H), 3.85(s, 3H), 3.65(t, 2H), 2.55(t, 2H), 2.35(s, 6H), 2.15(s, 3H), 1.98(t, 2H)

Example 336

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine 2maleic acid

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine(100mg, 0.18mmol) prepared from Example 317 in ethanol(1ml) was added maleic acid(43mg, 0.36mmol) and the reaction mixture was stirred for 2hr at room temperature. The reaction solution was concentrated *in vacuo* and the solid was washed with diethyl ether to give the title compound(100mg, 71.5%).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 9.10(bs, 1H), 7.90(d, 2H), 7.60(s, 1H), 7.30-7.50(m, 5H), 7.20(t, 2H), 6.75(d, 1H), 6.20(s, 4H), 5.60(s, 2H), 4.70(s, 2H), 3.80(s, 3H), 3.45(t, 2H), 2.50(t, 2H), 1.95(s, 3H), 1.85(t, 2H)

Example 337

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine 2malic acid

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine(100mg, 0.18mmol) prepared from Example 317 in ethanol(1ml) was added malic acid(50mg, 0.36mmol), and the reaction mixture was stirred for 2hr at room temperature. The reaction solution was concentrated *in vacuo* and the solid was washed with diethyl ether to give the title compound(100mg, 68.3%).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 7.95(s, 1H), 7.85(d, 2H), 7.60(s, 1H), 7.10-7.40(m,

7H), 6.90(s, 1H), 6.75(d, 1H), 5.35(s, 2H), 4.70(s, 2H), 4.25(t, 2H), 3.80(s, 3H), 3.40(t, 2H), 2.35-2.70(m, 6H), 1.95(s, 3H), 1.80(t, 2H)

Example 338

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine 2malonic acid

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine(100mg, 0.18mmol) prepared from Example 317 in ethanol(1ml) was added malonic acid(36mg, 0.36mmol) and the reaction mixture was stirred for 2hr at room temperature. The reaction solution was concentrated *in vacuo* and the solid was washed with diethyl ether to give the title compound(100mg, 73.8%).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 8.20(s, 1H), 7.85(d, 2H), 7.60(d, 1H), 7.10-7.40(m, 7H), 7.05(s, 1H), 6.75(d, 1H), 5.40(s, 2H), 4.70(s, 2H), 3.80(s, 3H), 3.45(t, 2H), 3.20(s, 4H), 2.40(t, 2H), 1.95(s, 3H), 1.80(t, 2H)

Example 339

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine 2tartaric acid

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine(100mg, 0.18mmol) prepared from Example 317 in ethanol(1ml) was added tartaric acid(53mg, 0.36mmol) and the reaction mixture was stirred for 2hr at room temperature. The reaction solution was concentrated *in vacuo* and the solid was washed with diethyl ether to give the title compound(100mg, 65.7%).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(CD_3OD-d_4) δ 8.50(s, 1H), 7.78(d, 2H), 7.60(d, 1H), 7.20-7.40(m, 8H), 6.78(d, 1H), 5.45(s, 2H), 4.78(s, 2H), 4.48(s, 4H), 3.87(s, 3H), 3.55(t, 2H), 2.50(t, 2H), 1.90(s, 5H)

Example 340

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine 2citric acid

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine(100mg, 0.18mmol) prepared from Example 317 in ethanol(1ml) was added citric acid(62mg, 0.36mmol) and the reaction mixture was stirred for 2hr at room temperature. The reaction solution was concentrated *in vacuo* and the solid was washed with diethyl ether to give the title compound(100mg, 58.9%).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 8.05(s, 1H), 7.82(d, 2H), 7.58(d, 1H), 7.10-7.40(m, 7H), 6.95(s, 1H), 6.70(d, 1H), 5.38(s, 2H), 4.70(s, 2H), 3.80(s, 3H), 3.55(t, 2H), 2.70(q, 8H), 2.40(t, 2H), 1.95(s, 3H), 1.80(t, 2H)

Example 341

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-hydroxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine

A solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-methyl]isothiocarbamoyl-3-chlorobenzylamine 2HCl(2.93g, 4.74mmol) prepared from Example 333 in 6N-HCl(20ml) was stirred for 24hr at room temperature. The reaction mixture was neutralized with a solution of saturated

$NaHCO_3$ and the organic layer was dried over anhydrous sodium sulfate. The solution was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(135mg).

^{1}H-NMR(DMSO-d_6) δ 7.60(d, 1H), 7.48(s, 1H), 7.17-7.35(m, 4H), 6.99-7.08(m, 4H), 6.87(s, 1H), 6.55(d, 1H), 5.08(s, 2H), 4.67(s, 2H), 3.44(t, 2H), 2.30(t, 2H), 2.02(s, 3H), 1.85(m, 2H)

Example 342

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-(1-propyl)]isothiocarbamoyl-2-trifluoromethylbenzylamine

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine(30mg, 0.053mmol) prepared from Example 214 in methanol(1ml) was added 1-iodopropane(45.2mg, 0.266mmol). The mixture was stirred for 24hr at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(10mg, 31%).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.75-7.76(m, 1H), 7.49-7.70(m, 5H), 7.35-7.43(m, 2H), 7.21-7.27(m, 1H), 7.08(d, 2H), 6.90(s, 1H), 6.68(d, 1H), 5.11(s, 2H), 5.00(s, 2H), 3.93(s, 3H), 3.51(t, 2H), 2.32-2.40(m, 2H), 2.26(t, 2H), 1.91-1.98(m, 2H), 1.23-1.44(m, 2H), 0.77(t, 3H)

Example 343-346

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine prepared from Example

214 was reacted with the corresponding alkyl or allyl iodide derivatives under the same condition as described in Example 342 to give the title compounds.

Example 343

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-(1-butyl)]isothiocarbamoyl-2-trifluoromethylbenzylamine

Yield=26%

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.75-7.76(m, 1H), 7.49-7.69(m, 5H), 7.35-7.42(m, 2H), 7.19-7.27(m, 1H), 7.07(d, 2H), 6.90(s, 1H), 6.67(d, 1H), 5.10(s, 2H), 4.99(s, 2H), 3.92(s, 3H), 3.51(t, 2H), 2.24-2.39(m, 4H), 1.90-1.97(m, 2H), 1.25-1.36(m, 2H), 1.13-1.20(m, 2H), 0.77(t, 3H)

Example 344

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-(1-pentyl)]isothiocarbamoyl-2-trifluoromethylbenzylamine

Yield=32%

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.75-7.76(m, 1H), 7.49-7.69(m, 5H), 7.35-7.42(m, 2H), 7.20-7.27(m, 1H), 7.07(d, 2H), 6.89(s, 1H), 6.68(d, 1H), 5.11(s, 2H), 5.00(s, 2H), 3.92(s, 3H), 3.51(t, 2H), 2.24-2.39(m, 4H), 1.90-1.97(m, 2H), 1.26-1.37(m, 2H), 1.12-1.14(m, 4H), 0.81(t, 3H)

Example 345

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-(1-hexyl)]isothiocarbamoyl-2-trifluoromethylbenzylamine

Yield=26%

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.74-7.75(m, 1H), 7.49-7.69(m, 5H), 7.34-7.41(m, 2H), 7.20-7.27(m, 1H), 7.06(d, 2H), 6.88(s, 1H), 6.67(d, 1H), 5.10(s, 2H), 4.99(s,

2H), 3.92(s, 3H), 3.50(t, 2H), 2.23-2.38(m, 4H), 1.90-1.97(m, 2H), 1.21-1.32(m, 4H), 1.12-1.17(m, 4H), 0.83(t, 3H)

Example 346

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-allyl]isothiocarbamoyl-2-trifluoromethylbenzylamine

Yield=29%

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.77-7.79(m, 1H), 7.51-7.69(m, 5H), 7.36-7.42(m, 2H), 7.23-7.29(m, 1H), 7.07(d, 2H), 6.90(s, 1H), 6.70(d, 1H), 5.45-5.68(m, 1H), 5.11(s, 2H), 5.04(s, 2H), 4.99(s, 2H), 3.93(s, 3H), 3.50(t, 2H), 2.94(d, 2H), 2.35(t, 2H), 1.90-1.97(m, 2H)

Example 347

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-benzyl]isothiocarbamoyl-2-trifluoromethylbenzylamine

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine(30mg, 0.053mmol) prepared from Example 214 in methanol(1ml) was added benzyl bromide(45.5mg, 0.266mmol). The mixture was stirred for 24hr at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: dichloromethane/methanol=40/1, v/v) to give the title compound(3.3mg).

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.83(s, 1H), 7.53-7.61(m, 1H), 7.19-7.46(m, 7H), 6.99-7.03(m, 5H), 6.82(s, 1H), 6.69(d, 1H), 5.04(s, 2H), 4.78(s, 2H), 3.91(s, 3H), 3.45(s, 2H), 3.32(t, 2H), 2.23(t, 2H), 1.72-1.78(m, 2H)

Example 348-352

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine prepared from Example 214 was reacted with the corresponding benzyl bromide derivatives under the same condition as described in Example 347 to give the title compounds.

Example 348

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-(2-cyanobenzyl)]isothiocarbamoyl-2-trifluoromethylbenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.80(s, 1H), 7.51-7.62(m, 4H), 7.40-7.45(m, 2H), 7.21-7.33(m, 3H), 7.02-7.15(m, 4H), 6.78(s, 1H), 6.68(dd, 1H), 5.07(s, 2H), 4.81(s, 2H), 3.90(s, 3H), 3.67(s, 2H), 3.37(t, 2H), 2.28(t, 2H), 1.75-1.83(m, 2H)

Example 349

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-(3-cyanobenzyl)]isothiocarbamoyl-2-trifluoromethylbenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.84(d, 1H), 7.58-7.68(m, 2H), 7.42-7.52(m, 2H), 7.24-7.38(m, 6H), 7.05-7.09(m, 4H), 6.87(s, 1H), 6.73(d, 1H), 5.10(s, 2H), 4.82(s, 2H), 3.96(s, 3H), 3.48(s, 2H), 3.40(t, 2H), 2.30(t, 2H), 1.79-1.85(m, 2H)

Example 350

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-(4-cyanobenzyl)]isothiocarbamoyl-2-trifluoromethylbenzylamine

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.85(s, 1H), 7.26-7.68(m, 8H), 7.00-7.14(m, 6H), 6.89(s, 1H), 6.73(d, 1H), 5.09(s, 2H), 4.83(s, 2H), 3.96(s, 3H), 3.49(s, 2H), 3.39(t, 2H), 2.29(t, 2H), 1.79-1.86(m, 2H)

Example 351

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-(4-nitrobenzyl)]isothiocarbamoyl-2-trifluoromethylbenzylamine

Yield=30%

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 8.03(d, 2H), 7.85(d, 1H), 7.66(s, 1H), 7.61(d, 2H), 7.50(s, 1H), 7.30-7.39(m, 3H), 7.16(d, 2H), 7.05(d, 2H), 6.93-7.00(m, 1H), 6.87(s, 1H), 6.73(d, 1H), 5.08(s, 2H), 4.83(s, 2H), 3.95(s, 3H), 3.53(s, 2H), 3.40(t, 2H), 2.29(t, 2H), 1.78-1.86(m, 2H)

Example 352

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-[(2-methoxypyridin-5-yl)-S-(3-methoxybenzyl)]isothiocarbamoyl-2-trifluoromethylbenzylamine

Yield=26%

R_f=0.35(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR($CDCl_3$) δ 7.86(d, 1H), 7.57-7.65(m, 3H), 7.26-7.49(m, 4H), 7.03-7.19(m, 4H), 6.86(s, 1H), 6.61-6.75(m, 4H), 5.08(s, 2H), 4.83(s, 2H), 3.96(s, 3H), 3.74(s, 3H), 3.46(s, 2H), 3.38(t, 2H), 2.27(t, 2H), 1.75-1.84(m, 2H)

Example 353

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine 2HCl

A solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine(500mg, 0.90mmol) prepared from Example 214 in dichloromethane(5ml) was bubbled HCl gas at ice bath for 3 minute. The reaction solution was poured into diethyl ether(50ml) and the resulting solid was filtered to give the title compound(150mg, 97%).

R_f=0.30(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(CD_3OD) δ 7.39-9.05(m, 13H), 5.60(s, 2H), 5.29(s, 2H), 4.11(s, 3H),3.80(t, 2H), 2.64(t, 2H), 2.07(m, 2H)

Example 354

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine citric acid

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine(100mg, 0.18mmol) prepared from Example 214 in ethanol(1ml) was added citric acid(69mg, 0.36mmol) and the reaction mixture was stirred for 4hr at room temperature. Diethyl ether(5ml) was added and the resulting solid was filtered to give the title compound(100mg, 58.7%).

R_f=0.30(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 9.38(s, 1H), 8.00(m, 2H), 7.50-7.80(m, 6H), 7.35(d, 1H), 7.7.27(d, 2H), 6.90(s, 1H), 6.83(d, 1H), 5.38(s, 2H), 5.24(s, 2H), 3.90(s, 3H), 3.65(t, 2H), 2.75(q, 4H), 2.42(t, 2H), 1.95(p, 2H)

Example 355

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine maleic acid

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine(100mg, 0.18mmol) prepared from Example 214 in ethanol(1ml) was added maleic acid(42mg, 0.36mmol) and the reaction mixture was stirred for 4hr at room temperature. Diethyl ether(5ml) was added and the resulting solid was filtered to give the title

compound(100mg, 58.9%).

R_f=0.30(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 9.38(s, 1H), 8.85(s, 1H), 8.00(s, 1H), 7.50-7.80(m, 6H), 7.45(s, 2H), 7.41(s, 1H), 7.37(d, 1H), 6.83(d, 1H), 6.15(s, 2H), 5.52(s, 2H), 5.24(s, 2H), 3.90(s, 3H), 3.70(t, 2H), 2.50(t, 2H), 2.00(p, 2H)

Example 356

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine malic acid

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine(100mg, 0.18mmol) prepared from Example 214 in ethanol(1ml) was added malic acid(49mg, 0.36mmol) and the reaction mixture was stirred for 4hr at room temperature. Diethyl ether(5ml) was added and the resulting solid was filtered to give the title compound(100mg, 58.9%).

R_f=0.30(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 9.38(s, 1H), 8.00(s, 1H), 7.50-7.80(m, 7H), 7.35(d, 1H), 7.25(d, 2H), 6.82(d+s, 2H), 5.35(s, 2H), 5.24(s, 2H), 4.30(t, 1H), 3.90(s, 3H), 3.70(t, 2H), 2.50-2.70(m, 4H), 2.43(t, 2H), 1.97(p, 2H)

Example 357

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine malonic acid

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine(100mg, 0.18mmol) prepared from Example 214 in ethanol(1ml) was added malonic acid(37mg, 0.36mmol)

and the reaction mixture was stirred for 4hr at room temperature. Diethyl ether(5ml) was added and the resulting solid was filtered to give the title compound(100mg, 59.9%).

R_f=0.30(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 9.38(s, 1H), 8.00(m, 2H), 7.50-7.80(m, 6H), 7.35(d, 1H), 7.27(d, 2H), 6.92(s, 1H), 6.82(d, 1H), 5.38(s, 2H), 5.24(s, 2H), 3.90(s, 3H), 3.70(t, 2H), 3.20(s, 2H), 2.43(t, 2H), 1.97(p, 2H)

Example 358

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine 2methanesulfonic acid

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine(100mg, 0.18mmol) prepared from Example 214 in ethanol(1ml) was added methanesulfonic acid(23ul, 0.36mmol) and the reaction mixture was stirred for 4hr at room temperature. diethyl ether(5ml) was added and the resulting solid was filtered to give the title compound(100mg, 60.9%).

R_f=0.30(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 9.42(s, 1H), 9.26(s, 1H), 8.05(s, 1H), 7.90(d, 2H), 7.62-7.82(m, 4H), 7.42-7.62(m, 3H), 7.35(d, 1H), 6.90(d, 1H), 5.60(s, 2H), 5.24(s, 2H), 3.90(s, 3H), 3.70(t, 2H), 2.43(t, 2H), 2.61(s, 6H), 2.00(p, 2H)

Example 359

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine oxalic acid

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl

)thiocarbamoyl-2-trifluoromethylbenzylamine(100mg, 0.18mmol) prepared from Example 214 in ethanol(1ml) was added oxalic acid(45mg, 0.36mmol) and the reaction mixture was stirred for 4hr at room temperature. The reaction solution was treated with diethyl ether(5ml) and the resulting solid was filtered to give the title compound(100mg, 59.9%).

R_f=0.30(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 9.40(s, 1H), 8.43(m, 1H), 8.00(s, 1H), 7.50-7.90(m, 6H), 7.35(d, 3H), 7.20(d, 1H), 6.82(d, 1H), 5.45(s, 2H), 5.24(s, 2H), 3.90(s, 3H), 3.70(t, 2H), 2.43(t, 2H), 2.00(p, 2H)

Example 360

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine tartaric acid

To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine(100mg, 0.18mmol) prepared from Example 214 in ethanol(1ml) was added tartaric acid(54mg, 0.36mmol) and the reaction mixture was stirred for 4hr at room temperature. The reaction solution was treated with diethyl ether(5ml) and the resulting solid was filtered to give the title compound(100mg, 58.9%).

R_f=0.30(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 9.40(s, 1H), 8.02(s, 1H), 7.50-7.90(m, 7H), 7.35(d, 1H), 7.25(d, 2H), 6.82(s+d, 2H), 5.38(s, 2H), 5.27(s, 2H), 4.38(s, 2H), 3.90(s, 3H), 3.70(t, 2H), 2.43(t, 2H), 2.00(p, 2H)

Example 361

N-{3-[1-(4-Cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine 2acetic acid

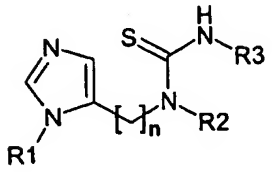
To a solution of N-{3-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]}propyl-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2-trifluoromethylbenzylamine(100mg, 0.18mmol) prepared from Example 214 in ethanol(1ml) was added acetic acid(21mg, 0.36mmol) and the reaction mixture was stirred for 4hr at room temperature. The reaction solution was diluted with diethyl ether(5ml) and the resulting solid was filtered to give the title compound(100mg, 61.4%).

R_f=0.30(dichloromethane/methanol=20/1, v/v)

^{1}H-NMR(DMSO-d_6) δ 9.40(s, 1H), 8.02(s, 1H), 7.50-7.90(m, 7H), 7.35(d, 1H), 7.25(d, 2H), 6.82(s+d, 2H), 5.38(s, 2H), 5.27(s, 2H), 4.38(s, 2H), 3.90(s, 3H), 3.70(t, 2H), 2.43(t, 2H), 2.00(p, 2H), 1.98(s, 6H)

The structures of the compouds prepared in Examples are shown in Tables I to III.

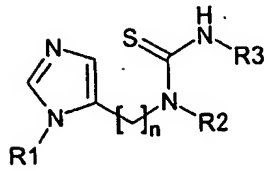
Table I. (Thiocarbamoyl derivatives)



Ex.	n	R^1	R^2	R^3
1	2	4-cyanobenzyl	2-trifluoromethylbenzyl	4-methoxyphenyl
2	2	4-cyanobenzyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
3	2	4-cyanobenzyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl(2HCl)
4	2	4-cyanobenzyl	2-trifluoromethylbenzyl	Allyl
5	2	4-cyanobenzyl	2-trifluoromethylbenzyl	Isobutyl
6	2	4-cyanobenzyl	2-trifluoromethylbenzyl	2-methoxyethyl
7	2	4-cyanobenzyl	2-trifluoromethylbenzyl	3-ethoxypropyl
8	2	4-cyanobenzyl	2-trifluoromethylbenzyl	Butyl
9	2	4-cyanobenzyl	2-trifluoromethylbenzyl	Cyclopentyl
10	2	4-cyanobenzyl	2-trifluoromethylbenzyl	Cyclohexyl
11	2	4-cyanobenzyl	2-trifluoromethylbenzyl	3-fluorophenyl
12	2	4-cyanobenzyl	2-trifluoromethylbenzyl	2-methoxyphenyl
13	2	4-cyanobenzyl	2-trifluoromethylbenzyl	4-methylphenyl
14	2	4-cyanobenzyl	2-trifluoromethylbenzyl	4-nitrophenyl
15	2	4-cyanobenzyl	2-trifluoromethylbenzyl	3-trifluoromethylphenyl
16	2	4-cyanobenzyl	2-trifluoromethylbenzyl	3-chloro-4-methylphenyl
17	2	4-cyanobenzyl	2-trifluoromethylbenzyl	Benzyl
18	2	4-cyanobenzyl	2-trifluoromethylbenzyl	2-phenylphenyl
19	2	4-cyanobenzyl	2-trifluoromethylbenzyl	2-chlorophenyl
20	2	4-cyanobenzyl	2-trifluoromethylbenzyl	2-(N,N-dimethylamino)ethyl
21	2	4-cyanobenzyl	2-trifluoromethylbenzyl	4-trifluoromethoxyphenyl
22	2	4-cyanobenzyl	2-trifluoromethylbenzyl	3-hydroxy-4-methoxyphenyl
23	2	4-cyanobenzyl	2-trifluoromethylbenzyl	4-methylthiophenyl
24	2	4-cyanobenzyl	2-trifluoromethylbenzyl	1-naphthyl
25	2	4-cyanobenzyl	2-trifluoromethylbenzyl	2,2-dimethyl-3,3-dimethylbutyl
26	2	4-cyanobenzyl	2-trifluoromethylbenzyl	2-phenylethyl
27	2	4-cyanobenzyl	2-trifluoromethylbenzyl	Phenyl
28	2	4-cyanobenzyl	2-trifluoromethylbenzyl	t-butyl
29	2	4-cyanobenzyl	2-trifluoromethylbenzyl	Butyl
30	2	4-cyanobenzyl	2-trifluoromethylbenzyl	Propyl

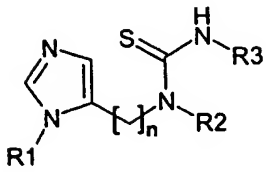
5

Table I. (continued)



Ex.	n	R^1	R^2	R^3
31	2	4-cyanobenzyl	2-trifluoromethylbenzyl	Ethyl
32	2	4-cyanobenzyl	2-trifluoromethylbenzyl	Adamantyl
33	2	4-cyanobenzyl	2-trifluoromethylbenzyl	Methyl
34	2	4-cyanobenzyl	2-trifluoromethylbenzyl	4-hydroxyphenyl
35	2	4-cyanobenzyl	2-trifluoromethylbenzyl	Benzoyl
36	2	4-cyanobenzyl	2-trifluoromethylbenzyl	2-pyrimidyl
37	2	4-cyanobenzyl	2-trifluoromethylbenzyl	1-piperidino
38	2	4-cyanobenzyl	2-trifluoromethylbenzyl	4-morpholino
39	2	4-cyanobenzyl	2-trifluoromethylbenzyl	4-methyl-1-piperazinyl
41	2	4-cyanobenzyl	2,3-dichlorobenzyl	4-methyoxyphenyl
42	2	4-cyanobenzyl	2,3-dichlorobenzyl	2-methoxypridin-5-yl
43	2	4-cyanobenzyl	2,3-dichlorobenzyl	3-fluorophenyl
44	2	4-cyanobenzyl	2,3-dichlorobenzyl	4-chlorophenyl
45	2	4-cyanobenzyl	2,3-dichlorobenzyl	4-methylphenyl
46	2	4-cyanobenzyl	2,3-dichlorobenzyl	4-nitrophenyl
47	2	4-cyanobenzyl	2,3-dichlorobenzyl	3-chloro-4-methylphenyl
48	2	4-cyanobenzyl	2,3-dichlorobenzyl	3-chlorophenyl
49	2	4-cyanobenzyl	2,3-dichlorobenzyl	4-methylthiophenyl
50	2	4-cyanobenzyl	2,3-dichlorobenzyl	Cyclohexyl
51	2	4-cyanobenzyl	2,3-dichlorobenzyl	Ethoxycarbonyl
52	2	4-cyanobenzyl	2,3-dichlorobenzyl	2-naphthyl
53	2	4-cyanobenzyl	2,3-dichlorobenzyl	phenyl
54	2	4-cyanobenzyl	2,3-dichlorobenzyl	2-methylphenyl
55	2	4-cyanobenzyl	2,3-dichlorobenzyl	4-fluorophenyl
56	2	4-cyanobenzyl	2-chlorobenzyl	4-chlorophenyl
57	2	4-cyanobenzyl	2-chlorobenzyl	3-chloro-4-methylphenyl
58	2	4-cyanobenzyl	2-chlorobenzyl	4-methoxypphenyl
59	2	4-cyanobenzyl	2-chlorobenzyl	2-methoxypyridin-5-yl
60	2	4-cyanobenzyl	3-chlorobenzyl	3-fluorophenyl

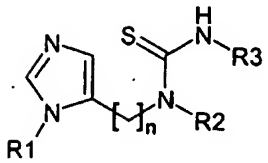
Table I. (continued)



Ex.	n	R^1	R^2	R^3
61	2	4-cyanobenzyl	3-chlorobenzyl	4-bromophenyl
62	2	4-cyanobenzyl	3-chlorobenzyl	4-methylphenyl
63	2	4-cyanobenzyl	3-chlorobenzyl	3-chloro-4-methylphenyl
64	2	4-cyanobenzyl	3-chlorobenzyl	3-chlorophenyl
65	2	4-cyanobenzyl	3-chlorobenzyl	4-trifluoromethylphenyl
66	2	4-cyanobenzyl	3-chlorobenzyl	4-methoxyphenyl
67	2	4-cyanobenzyl	3-chlorobenzyl	2-methoxypyridin-5-yl
68	2	4-cyanobenzyl	2-fluorobenzyl	3-fluorophenyl
69	2	4-cyanobenzyl	2-fluorobenzyl	4-methylphenyl
70	2	4-cyanobenzyl	2-fluorobenzyl	3-chloro-4-methylphenyl
71	2	4-cyanobenzyl	2-fluorobenzyl	4-methylthiophenyl
72	2	4-cyanobenzyl	2-fluorobenzyl	4-methoxyphenyl
73	2	4-cyanobenzyl	2-fluorobenzyl	2-methoxypyridin-5-yl
74	2	4-cyanobenzyl	3-fluorobenzyl	4-fluorophenyl
75	2	4-cyanobenzyl	3-fluorobenzyl	4-methylphenyl
76	2	4-cyanobenzyl	3-fluorobenzyl	3-chloro-4-methylphenyl
77	2	4-cyanobenzyl	3-fluorobenzyl	3-chlorophenyl
78	2	4-cyanobenzyl	3-fluorobenzyl	4-methoxyphenyl
79	2	4-cyanobenzyl	3-fluorobenzyl	2-methoxypyridin-5-yl
80	2	4-cyanobenzyl	3-fluorobenzyl	4-methylthiophenyl
81	2	4-cyanobenzyl	3-fluorobenzyl	3-trifluoromethylphenyl
82	2	4-cyanobenzyl	2-methylbenzyl	3-chloro-4-methylphenyl
83	2	4-cyanobenzyl	2-methylbenzyl	4-fluorophenyl
84	2	4-cyanobenzyl	2-methylbenzyl	3-fluorophenyl
85	2	4-cyanobenzyl	2-methylbenzyl	4-methylphenyl
86	2	4-cyanobenzyl	2-methylbenzyl	3-trifluoromethylphenyl
87	2	4-cyanobenzyl	2-methylbenzyl	3-chlorophenyl
88	2	4-cyanobenzyl	2-methylbenzyl	4-methoxyphenyl
89	2	4-cyanobenzyl	2-methylbenzyl	2-methoxypyridin-5-yl
90	2	4-cyanobenzyl	2,3-difluorobenzyl	3-fluorophenyl

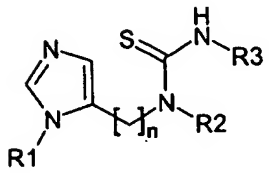
5

Table I. (continued)



Ex.	n	R^1	R^2	R^3
91	2	4-cyanobenzyl	2,3-difluorobenzyl	4-fluorophenyl
92	2	4-cyanobenzyl	2,3-difluorobenzyl	4-methylphenyl
93	2	4-cyanobenzyl	2,3-difluorobenzyl	3-chloro-4-methylphenyl
94	2	4-cyanobenzyl	2,3-difluorobenzyl	3-chlorophenyl
95	2	4-cyanobenzyl	2,3-difluorobenzyl	4-trifluoromethylphenyl
96	2	4-cyanobenzyl	2,3-difluorobenzyl	4-methoxyphenyl
97	2	4-cyanobenzyl	2,3-difluorobenzyl	2-methoxypyridin-5-yl
98	2	4-cyanobenzyl	2,6-difluorobenzyl	4-methylphenyl
99	2	4-cyanobenzyl	2,6-difluorobenzyl	4-fluorophenyl
100	2	4-cyanobenzyl	2,6-difluorobenzyl	3-chloro-4-methylphenyl
101	2	4-cyanobenzyl	2,6-difluorobenzyl	4-methoxyphenyl
102	2	4-cyanobenzyl	2,6-difluorobenzyl	2-methoxypyridin-5-yl
103	2	4-cyanobenzyl	4-trifluoromethylbenzyl	4-fluorophenyl
104	2	4-cyanobenzyl	4-trifluoromethylbenzyl	4-chlorophenyl
105	2	4-cyanobenzyl	4-trifluoromethylbenzyl	3-chloro-4-methylphenyl
106	2	4-cyanobenzyl	4-trifluoromethylbenzyl	3-chlorophenyl
107	2	4-cyanobenzyl	4-trifluoromethylbenzyl	4-methoxyphenyl
108	2	4-cyanobenzyl	4-trifluoromethylbenzyl	2-methoxypyridin-5-yl
109	2	4-cyanobenzyl	4-trifluoromethylbenzyl	3-fluorophephenyl
110	2	4-cyanobenzyl	(1-methyl-1H-pyrrol-2-yl)methyl	3-fluorophenyl
111	2	4-cyanobenzyl	(1-methyl-1H-pyrrol-2-yl)methyl	4-chlorophenyl
112	2	4-cyanobenzyl	(1-methyl-1H-pyrrol-2-yl)methyl	3-chlorophenyl
113	2	4-cyanobenzyl	(1-methyl-1H-pyrrol-2-yl)methyl	4-methoxylphenyl
114	2	4-cyanobenzyl	(1-methyl-1H-pyrrol-2-yl)methyl	2-methoxypyridin-5-yl
115	2	4-cyanobenzyl	(1H-indol-3-yl)methyl	4-fluorophenyl
116	2	4-cyanobenzyl	(1H-indol-3-yl)methyl	3-chlorophenyl
117	2	4-cyanobenzyl	(1H-indol-3-yl)methyl	2-phenylethyl
118	2	4-cyanobenzyl	(1H-indol-3-yl)methyl	4-methoxyphenyl
119	2	4-cyanobenzyl	(1H-indol-3-yl)methyl	2-methoxypyridin-5-yl
120	2	4-cyanobenzyl	(6-methyl-pyridin-2-yl)methyl	3-fluorophenyl

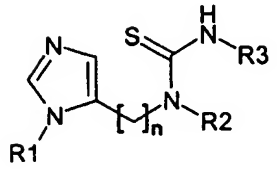
Table I. (continued)



Ex.	n	R^1	R^2	R^3
121	2	4-cyanobenzyl	(6-methyl-pyridin-2-yl)methyl	3-chloro-4-methylphenyl
122	2	4-cyanobenzyl	(6-methyl-pyridin-2-yl)methyl	3-chlorophenyl
123	2	4-cyanobenzyl	(6-methyl-pyridin-2-yl)methyl	4-methylthiophenyl
124	2	4-cyanobenzyl	(6-methyl-pyridin-2-yl)methyl	4-methoxyphenyl
125	2	4-cyanobenzyl	(6-methyl-pyridin-2-yl)methyl	2-methylpyridin-5-yl
126	2	4-cyanobenzyl	(2-chloro-pyridin-3-yl)methyl	3-fluorophenyl
127	2	4-cyanobenzyl	(2-chloro-pyridin-3-yl)methyl	3-chloro-4-methylphenyl
128	2	4-cyanobenzyl	(2-chloro-pyridin-3-yl)methyl	3-trifluoromethylphenyl
129	2	4-cyanobenzyl	(1-methyl-1H-indol-3-yl)methyl	3-fluorophenyl
130	2	4-cyanobenzyl	(1-methyl-1H-indol-3-yl)methyl	3-chloro-4-methylphenyl
131	2	4-cyanobenzyl	(1-methyl-1H-indol-3-yl)methyl	3-chlorophenyl
132	2	4-cyanobenzyl	(3-chloro-pyridin-4-yl)methyl	4-chlorophenyl
133	2	4-cyanobenzyl	(3-chloro-pyridin-4-yl)methyl	3-chloro-4-methylphenyl
134	2	4-cyanobenzyl	(3-chloro-pyridin-4-yl)methyl	2-methoxypyridin-5-yl
135	2	4-cyanobenzyl	(2,6-dichloropyridin-3-yl)methyl	3-fluorophenyl
136	2	4-cyanobenzyl	(2,6-dichloropyridin-3-yl)methyl	3-chloro-4-methylphenyl
137	2	4-cyanobenzyl	(2,6-dichloropyridin-3-yl)methyl	3-trifluoromethylphenyl
138	2	4-cyanobenzyl	(2,6-dichloropyridin-3-yl)methyl	4-methoxyphenyl
139	2	4-cyanobenzyl	(2,6-dichloropyridin-3-yl)methyl	2-methoxypyridin5-yl
140	2	4-cyanobenzyl	(5-methoxy-1H-indol-3-yl)methyl	3-fluorophenyl
141	2	4-cyanobenzyl	(5-methoxy-1H-indol-3-yl)methyl	4-methylphenyl
142	2	4-cyanobenzyl	(5-methoxy-1H-indol-3-yl)methyl	3-chlorophenyl
143	2	4-cyanobenzyl	(5-methoxy-1H-indol-3-yl)methyl	4-methoxylphenyl
144	2	4-cyanobenzyl	(5-methoxy-1H-indol-3-yl)methyl	2-methoxypyridin-5-yl
145	2	4-cyanobenzyl	(2-methyl-1H-indol-3-yl)methyl	3-fluorophenyl
146	2	4-cyanobenzyl	(quinolin-4-yl)methyl	3-chloro-4-methylphenyl
147	2	4-cyanobenzyl	(quinolin-4-yl)methyl	2-phenylethyl
148	2	4-cyanobenzyl	(quinolin-4-yl)methyl	2-methoxypyridin-5-yl
149	2	4-cyanobenzyl	(6-chloropyridin-2-yl)methyl	3-chloro-4-methylphenyl
150	2	4-cyanobenzyl	(1-naphthyl)methyl	3-fluorophenyl

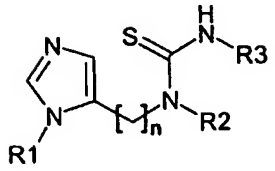
5

Table I. (continued)



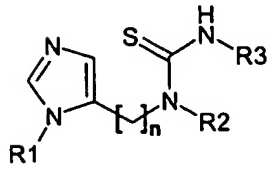
Ex.	n	R^1	R^2	R^3
151	2	4-cyanobenzyl	(1-naphthyl)methyl	4-methylphenyl
152	2	4-cyanobenzyl	(1-naphthyl)methyl	3-chloro-4-methylphenyl
153	2	4-cyanobenzyl	(1-naphthyl)methyl	3-chloropheny
154	2	4-cyanobenzyl	(1-naphthyl)methyl	4-methoxyphenyl
155	2	4-cyanobenzyl	(1-naphthyl)methyl	2-methylpyridin-5-yl
156	2	methyl	2-trifluoromethylbenzyl	3-chloro-4-methylphenyl
157	2	methyl	2,3-dichlorobenzyl	3-fluorophenyl
158	2	methyl	2,3-dichlorobenzyl	4-trifluoromethylphenyl
159	2	methyl	2,3-dichlorobenzyl	2-methoxypyridin-5-yl
160	2	(3,4-methylenedioxy)benzyl	2-trifluoromethylbenzyl	3-chloro-4-methylphenyl
161	2	(3,4-methylenedioxy)benzyl	2-trifluoromethylbenzyl	4-flurorophenyl
162	2	(3,4-methylenedioxy)benzyl	2-trifluoromethylbenzyl	4-methylphenyl
163	2	(3,4-methylenedioxy)benzyl	2-trifluoromethylbenzyl	4-trifluoromethylphenyl
164	2	(3,4-methylenedioxy)benzyl	2,3-dichlorobenzyl	4-chlorophenyl
165	2	(3,4-methylenedioxy)benzyl	2,3-dichlorobenzyl	3-fluorophenyl
166	2	(3,4-methylenedioxy)benzyl	2,3-dichlorobenzyl	4-fluorophenyl
167	2	(3,4-methylenedioxy)benzyl	2,3-dichlorobenzyl	3-hydroxy-4-methoxyphenyl
168	2	(3,4-methylenedioxy)benzyl	2,3-dichlorobenzyl	4-methylphenyl
169	2	(3,4-methylenedioxy)benzyl	2,3-dichlorobenzyl	Phenyl
170	2	4-cyanobenzyl	Butyl	3-chloro-4-methylphenyl
171	2	4-cyanobenzyl	Butyl	2,4-dimethoxyphenyl
172	2	4-cyanobenzyl	Butyl	2-methoxypyridin-5-yl
173	2	4-cyanobenzyl	2-butenyl	4-methylphenyl
174	2	4-cyanobenzyl	2-butenyl	4-methoxyphenyl
175	2	4-cyanobenzyl	2-butenyl	2-methoxypyridin-5-yl
176	2	4-cyanobenzyl	Cyclohexylmethyl	4-fluorophenyl
177	2	4-cyanobenzyl	Cyclohexylmethyl	4-methylphenyl
178	2	4-cyanobenzyl	Cyclohexylmethyl	3-trifluoromethylphenyl
179	2	4-cyanobenzyl	Cyclohexylmethyl	2-phenylethyl
180	2	4-cyanobenzyl	Isobutyl	3-chlorophenyl

Table I. (continued)



Ex.	n	R^1	R^2	R^3
181	2	4-cyanobenzyl	Isobutyl	2-phenylethyl
182	2	4-cyanobenzyl	Propyl	4-chlorophenyl
183	2	4-cyanobenzyl	Propyl	3-chloro-4-methylphenyl
184	2	4-cyanobenzyl	Propyl	4-trifluoromethylphenyl
185	2	4-cyanobenzyl	Pentyl	3-chlorophenyl
186	2	4-nitrobenzyl	2-trifluoromethylbenzyl	3-chlorophenyl
187	2	4-nitrobenzyl	2-trifluoromethylbenzyl	4-methoxyphenyl
188	2	4-nitrobenzyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
189	2	4-nitrobenzyl	2,3-dichlorobenzyl	3-chloro-4-methylphenyl
190	2	4-nitrobenzyl	2,3-dichlorobenzyl	3-chlorophenyl
191	2	4-nitrobenzyl	2,3-dichlorobenzyl	4-chlorophenyl
192	2	4-nitrobenzyl	2,3-dichlorobenzyl	3-fluorophenyl
193	2	4-nitrobenzyl	2,3-dichlorobenzyl	4-methoxyphenyl
194	2	4-nitrobenzyl	2,3-dichlorobenzyl	2-methoxypyridin
195	2	4-cyanobenzyl	α -methyl-(3-chloro)benzyl	4-methoxyphenyl
196	2	4-cyanobenzyl	α -methyl-(3-chloro)benzyl	2-methoxypyridin-5-yl
197	2	4-cyanobenzyl	α -methyl-(3-chloro)benzyl	4-fluorophenyl
198	2	4-cyanobenzyl	α -methyl-(3-fluoro)benzyl	4-methoxyphenyl
199	2	4-cyanobenzyl	α -methyl-(3-fluoro)benzyl	2-methoxypyridin-5-yl
200	2	4-cyanobenzyl	α -methyl-(3-fluoro)benzyl	4-chlorophenyl
201	2	4-cyanobenzyl	α -methyl-(3-fluoro)benzyl	4-methylphenyl
203	2	4-cyanobenzyl	2-methylphenyl	3-chlorophenyl
204	2	4-cyanobenzyl	2-methylphenyl	4-chlorophenyl
205	2	4-cyanobenzyl	2-methylphenyl	4-methylphenyl
206	3	4-cyanobenzyl	2-trifluoromethylbenzyl	3-chloro-4-methylphenyl
207	3	4-cyanobenzyl	2-trifluoromethylbenzyl	3-chlorophenyl
208	3	4-cyanobenzyl	2-trifluoromethylbenzyl	4-chlorophenyl
209	3	4-cyanobenzyl	2-trifluoromethylbenzyl	2, 4-dichlorophenyl
210	3	4-cyanobenzyl	2-trifluoromethylbenzyl	3-fluorophenyl

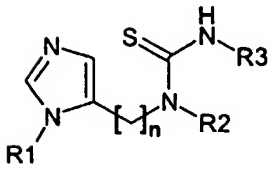
Table I. (continued)



Ex.	n	R_1	R_2	R_3
211	3	4-cyanobenzyl	2-trifluoromethylbenzyl	4-fluorophenyl
212	3	4-cyanobenzyl	2-trifluoromethylbenzyl	3-hydroxy-4-methylphenyl
213	3	4-cyanobenzyl	2-trifluoromethylbenzyl	4-methoxyphenyl
214	3	4-cyanobenzyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
215	3	4-cyanobenzyl	2-trifluoromethylbenzyl	2-methylphenyl
216	3	4-cyanobenzyl	2-trifluoromethylbenzyl	4-methylphenyl
217	3	4-cyanobenzyl	2-trifluoromethylbenzyl	phenyl
218	3	4-cyanobenzyl	2-trifluoromethylbenzyl	3-trifluoromethylphenyl
219	3	4-cyanobenzyl	2-trifluoromethylbenzyl	4-trifluoromethylphenyl
220	3	4-cyanobenzyl	2-trifluoromethylbenzyl	4-acetylphenyl
221	3	4-cyanobenzyl	2-trifluoromethylbenzyl	4-benzyloxyphenyl
222	3	4-cyanobenzyl	2-trifluoromethylbenzyl	3-bromophenyl
223	3	4-cyanobenzyl	2-trifluoromethylbenzyl	4-bromophenyl
224	3	4-cyanobenzyl	2-trifluoromethylbenzyl	3-chloro-6-methylphenyl
225	3	4-cyanobenzyl	2-trifluoromethylbenzyl	3-nitro-4-chlorophenyl
226	3	4-cyanobenzyl	2-trifluoromethylbenzyl	4-cyanophenyl
227	3	4-cyanobenzyl	2-trifluoromethylbenzyl	pentyl
228	3	4-cyanobenzyl	2-trifluoromethylbenzyl	4-N,N-dimethylamino-naphthyl-1-yl
229	3	4-cyanobenzyl	2-trifluoromethylbenzyl	4-ethoxylcarbonylphenyl
230	3	4-cyanobenzyl	2-trifluoromethylbenzyl	4-methylthiophenyl
231	3	4-cyanobenzyl	2-trifluoromethylbenzyl	1-naphthyl
232	3	4-cyanobenzyl	2-trifluoromethylbenzyl	Tetrahydrofuran-2-ylmethyl
233	3	4-cyanobenzyl	2-trifluoromethylbenzyl	3-phenylpropyl
234	3	4-cyanobenzyl	2-trifluoromethylbenzyl	Butyl
235	3	4-cyanobenzyl	2-trifluoromethylbenzyl	cyclohexyl
236	3	4-cyanobenzyl	2-trifluoromethylbenzyl	Cyclooctyl
237	3	4-cyanobenzyl	2-trifluoromethylbenzyl	cyclopropyl
238	3	4-cyanobenzyl	2-trifluoromethylbenzyl	Ethoxycarbonyl
239	3	4-cyanobenzyl	2-trifluoromethylbenzyl	Isobutyl
240	3	4-cyanobenzyl	2-trifluoromethylbenzyl	3-methoxypropyl

5

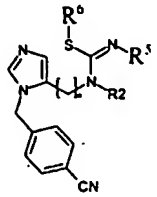
Table I. (continued)



Ex.	n	R^1	R^2	R^3
241	3	4-cyanobenzyl	2-trifluoromethylbenzyl	2-morpholin-4-ylethyl
242	3	4-cyanobenzyl	2,3-dichorobenzyl	4-fluorophenyl
243	3	4-cyanobenzyl	2,3-dichorobenzyl	3-chloro-4-methylphenyl
244	3	4-cyanobenzyl	2,3-dichorobenzyl	3-chlorophenyl
245	3	4-cyanobenzyl	2,3-dichorobenzyl	3-fluorophenyl
246	3	4-cyanobenzyl	2,3-dichorobenzyl	4-methoxyphenyl
247	3	4-cyanobenzyl	2,3-dichorobenzyl	2-methoxypyridin-5-yl
248	3	4-cyanobenzyl	2,3-dichorobenzyl	4-methylphenyl
249	3	4-cyanobenzyl	2,3-dichorobenzyl	3-trifluoromethylphenyl
250	3	4-cyanobenzyl	3-chlorobenzyl	3-chlorophenyl
251	3	4-cyanobenzyl	3-chlorobenzyl	4-chlorophenyl
252	3	4-cyanobenzyl	3-chlorobenzyl	4-methoxyphenyl
253	3	4-cyanobenzyl	3-chlorobenzyl	2-methoxypyridin-5-yl
254	3	4-cyanobenzyl	3-chlorobenzyl	2-methylphenyl
255	3	4-cyanobenzyl	3-chlorobenzyl	3-chloro-4-methylphenyl
256	3	4-cyanobenzyl	3-chlorobenzyl	3-fluorophenyl
257	3	4-cyanobenzyl	2-methylbenzyl	3-choro-4-methylphenyl
258	3	4-cyanobenzyl	2-methylbenzyl	4-fluorophenyl
259	3	4-cyanobenzyl	2-methylbenzyl	4-methylphenyl
260	3	4-cyanobenzyl	2-methylbenzyl	3-chlorophenyl
261	3	4-cyanobenzyl	2-methylbenzyl	3-fluorophenyl
262	3	4-cyanobenzyl	2-methylbenzyl	2-methoypyridin-5-yl
263	3	4-cyanobenzyl	(1-naphthyl)methyl	3-fluorophenyl
264	3	4-cyanobenzyl	(1-naphthyl)methyl	2-methoxypyridin-5-yl
265	3	4-cyanobenzyl	(1-naphthyl)methyl	3-chloro-4-methylphenyl
266	3	4-cyanobenzyl	(1-naphthyl)methyl	4-methoxyphenyl
267	4	4-cyanobenzyl	2-trifluoromethylbenzyl	4-chlorophenyl
268	4	4-cyanobenzyl	2-trifluoromethylbenzyl	4-fluorophenyl
269	4	4-cyanobenzyl	2-trifluoromethylbenzyl	4-methoxyphenyl
270	4	4-cyanobenzyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
271	1	4-cyanobenzyl	2-trifluoromethylbenzyl	4-methoxyphenyl
272	1	4-cyanobenzyl	2-trifluoromethylbenzyl	4-nitrophenyl
273	1	4-cyanobenzyl	2-trifluoromethylbenzyl	2-chlorophenyl

5

Table. II (Isothiocarbamoyl derivatives)

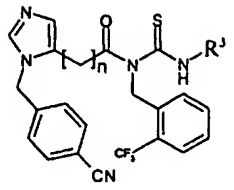


Ex	n	R^6	R^2	R^5
277	2	Methyl	2-trifluoromethylbenzyl	3-chloro-4-methylphenyl
278	2	Methyl	2-trifluoromethylbenzyl	Benzyl
279	2	Methyl	2-trifluoromethylbenzyl	4-methoylphenyl
280	2	Methyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
281	2	Methyl	2-trifluoromethylbenzyl	4-methylpenyl
282	2	Methyl	2,3-dichlorobenzyl	3-chloro-4-methylphenyl
283	2	Methyl	2,3-dichlorobenzyl	4-fluorophenyl
284	2	Methyl	2,3-dichlorobenzyl	4-methoxyphenyl
285	2	Methyl	3-chlorobenzyl	3-chloro-4-methylphenyl
286	2	Methyl	3-chlorobenzyl	3-flurorophenyl
287	2	Methyl	3-chlorobenzyl	4-methoxyphenyl
288	2	Methyl	3-chlorobenzyl	2-methoxypyridin-5-yl
289	2	Methyl	3-fluorobenzyl	3-chloro-4-methylphenyl
290	2	Methyl	3-fluorobenzyl	3-chlorophenyl
291	2	Methyl	3-fluorobenzyl	4-methoxylphenyl
292	2	Methyl	3-fluorobenzyl	3-trifluoromethylphenyl
293	2	Methyl	2,3-difluorobenzyl	3-cloro-4-methylphenyl
294	2	Methyl	2,3-difluorobenzyl	3-chlorophenyl
295	2	Methyl	2,3-difluorobenzyl	3-fluorophenyl
296	2	Methyl	2,3-difluorobenzyl	4-methoxyphenyl
297	2	Methyl	2,3-difluorobenzyl	2-methoxypyridin-5-yl
298	2	Methyl	4-trifluoromethylbenzyl	3-chloro-4-methylphenyl
299	2	Methyl	4-trifluoromethylbenzyl	3-fluorophenyl
300	2	Methyl	4-trifluoromethylbenzyl	4-fluorophenyl
301	2	Methyl	4-trifluoromethylbenzyl	4-methoxyphenyl
302	2	Methyl	1-naphthylmethyl	2-methoxypyridin-5-yl
303	3	Methyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
304	3	Methyl	2-trifluoromethylbenzyl	4-methoxyphenyl
305	3	Methyl	2-trifluoromethylbenzyl	3-chlorophenyl
306	3	Methyl	2-trifluoromethylbenzyl	3-fluorophenyl
307	3	Methyl	2,3-dichlorobenzyl	3-chloro-4-methylphenyl
308	3	Methyl	2,3-dichlorobenzyl	3-chlorophenyl
309	3	Methyl	2,3-dichlorobenzyl	3-fluorophenyl
310	3	Methyl	2,3-dichlorobenzyl	4-methoxyphenyl

Table. II (continued)

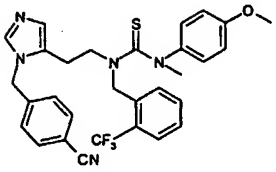
Ex.	n	R^6	R^2	R^5
311	3	Methyl	2,3-dichlorobenzyl	2-methoxypyridin-5-yl
312	3	Methyl	3-chlorobenzyl	3-chloro-4-methyphenyl
313	3	Methyl	3-chlorobenzyl	3-chlorophenyl
314	3	Methyl	3-chlorobenzyl	4-chlorophenyl
315	3	Methyl	3-chlorobenzyl	3-fluorophenyl
316	3	Methyl	3-chlorobenzyl	4-methoxyphenyl
317	3	Methyl	3-chlorobenzyl	2-methoxypyridin-5-yl
318	3	Methyl	2-methylbenzyl	3-chloro-4-methylphenyl
319	3	Methyl	2-methylbenzyl	3-chlorophenyl
320	3	Methyl	2-methylbenzyl	3-fluofophenyl
321	3	Methyl	2-methylbenzyl	2-methoxypyridin-5-yl
322	3	Methyl	2-methylbenzyl	4-methoxyphenyl
323	3	Methyl	(1-naphthyl)methyl	3-chloro-4-methylphenyl
324	3	Methyl	(1-naphthyl)methyl	3-fluorophenyl
325	3	Methyl	(1-naphthyl)methyl	4-methoxyphenyl
326	3	Methyl	(1-naphthyl)methyl	2-methoypyridin-5-yl
329	2	Methyl	2,3-dichlorobenzyl	4-fluorophenyl(HCl)
330	2	Methyl	2,3-dichlorobenzyl	4-methoxyphenyl(HCl)
331	2	Methyl	2,3-dichlorobenzyl	2-methoxypyridin-5-yl(HCl)
332	3	Methyl	3-chlorobenzyl	4-methoxyphenyl(HCl)
333	3	Methyl	3-chlorobenzyl	2-methoxypyridin-5-yl(2HCl)
334	3	Methyl	3-chlorobenzyl	2-methoxypyridin-5-yl(2oxalic acid)
335	3	Methyl	3-chlorobenzyl	2-methoxypyridin-5-yl(2methansulfonic acid)
336	3	Methyl	3-chlorobenzyl	2-methoxypyridin-5-yl (2maleic acid)
337	3	Methyl	3-chlorobenzyl	2-methoxypyridin-5-yl (2malic acid)
338	3	Methyl	3-chlorobenzyl	2-methoxypyridin-5-yl (2malonic acid)
339	3	Methyl	3-chlorobenzyl	2-methoxypyridin-5-yl (2tartatic acid)
340	3	Methyl	3-chlorobenzyl	2-methoxypyridin-5-yl (2citric acid)
341	3	Methyl	3-chlorobenzyl	2-hydroxypyridin-5-yl
342	3	1-propyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
343	3	1-butyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
344	3	1-pentyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
345	3	1-hexyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
346	3	Allyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
347	3	Benzyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
348	3	2-cyanobenzyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
349	3	3-cyanobenzyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
350	3	4-cyanobenzyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
351	3	4-nitrobenzyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl
352	3	3-methoxybenzyl	2-trifluoromethylbenzyl	2-methoxypyridin-5-yl

Table III



Ex.	n	R^3
274	1	4-methylphenyl
275	1	2-methoxypyridin-5-yl
276	2	4-methoxyphenyl

Structure of the compound of Example 202.



Assay 1: *In Vitro* Cell Growth Inhibition Assay

The viability of K-ras transformed cells was measured by using MTT colorimetric assay which is based on the conversion of MTT(3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) to MTT-formazan by mitochondrial enzyme. In brief, cells were dispensed within 96-well culture plate in 100 μ l culture medium at a density of 200 cells/well. Following 24 hours incubation at 37℃, 5% CO_2, 100% relative humidity, 100 μ l of culture medium containing compound or culture medium containing compound vehicle was dispensed within appropriate wells. Culture plates were then incubated for 4 days prior to addition of MTT reagent. MTT solution(5

mg/ml PBS) was added to the well in a concentration of 0.5 mg/ml. After incubation for 4 hours, mixed culture medium and MTT solution were carefully removed, then 100 μ l DMSO was added to the well to solubilize formazan. The absorbance of each well was measured using microculture plate reader at 570 nm. Measurements were performed in triplicate. Growth inhibition of 50%(IC_{50}) is calculated in terms of %T/C [(absorbance of treated cells/absorbance of control cells)× 100].

The results of the compounds shown in Table IV reflects their ability to inhibit K-ras transformed cell growth *in vitro*.

Assay 2 : *In vitro* inhibition of FPTase

Bovine brain cytosol was fractionated with ammonium sulfate and subjected the active fraction to ion exchange chromatography on a Mono Q column followed by gel filtration on sephacryl S-200. The Ras protein substrate, K-ras4B, is expressed in *Escherichia coli*. The donor of farnesyl residues to ras protein is [^{3}H] farnesyl pyrophosphate (FPP). The standard reaction mixture contained the following concentrations of components in a final volume of 50 μℓ ; 50 mM HEPES pH7.5, 5 mM $MgCl_2$, 5mM dithiothreitol (DTT), 10 μ M $ZnCl_2$, 0.2% n-Octyl-β -D-glucopyranoside and 0.6 μg K-ras4B. The mixture also contained 0.15 μ Ci of [^{3}H]FPP (16.0 Ci/mmol; Amersham Life Science) and 1.5 μg of partially purified farnesyl-protein transferase.

Test compounds were dissolved in 99.9% ethyl alcohol (EtOH). After incubation for 1 hr at 37℃ in 1.5 ml effendorf tubes, the reaction was stopped by the addition of 90 μℓ of 4% sodium dodecyl sulfate (SDS) and then 90 μℓ of 30% trichloroacetic acid (TCA). The tubes were left on ice for 45-60 minute and then the precipitates were transferred to Millipore multiscreen filtration 96-well plate with glass fiber C membrane (Millipore Corp.).

Following filtration using the multiscreen vacuum manifold, the wells were washed once with 200 μℓ of 4%SDS/6%TCA and five times with 200

μℓ of 6% TCA. Following removal of the bottom seal, excess washing fluid was blotted and the plates were allowed to dry before the filters were punched into 6 ml vials using the multiscreen punch. After punching, 5 ml of scintillation fluid (Packard) was added and radioactivity was determined by scintillation counting (Beckman LS5801). Dose-response curves for inhibitors used were duplicated at each drug concentration, and the IC_{50} estimations were made from Litchfield-Wilcoxon method.

The data presented below in Table IV reflects the ability of the test compound to inhibit ras farnesylation.

Table IV. Inhibition of K-ras transformed cell growth and *In vitro* FPTase

Compound	IC_{50}[a] (nM)	IC_{50}[b] (nM)	Compound	IC_{50}[a] (nM)	IC_{50}[b] (nM)
Example 1	0.1	1.60	Example 2	0.2	2.40
Example 4	0.7	14.9	Example 5	1.1	20.0
Example 6	0.5	20.0	Example 7	2.1	20.0
Example 8	3.6	9.02	Example 11	0.2	1.27
Example 12	2.8	5.45	Example 13	1.2	2.26
Example 14	0.4	0.83	Example 16	0.1	0.46
Example 17	2.3	19.8	Example 18	12.3	5.70
Example 21	5.6	NT[c]	Example 22	0.4	4.69
Example 23	0.3	1.71	Example 24	9.7	2.91
Example 27	3.4	10.57	Example 29	200	13.65
Example 34	24.0	NT	Example 37	NT	14.31
Example 39	NT	20.0	Example 40	NT	11.14
Example 43	0.2	0.87	Example 44	0.1	NT
Example 47	0.6	0.80	Example 48	0.3	0.92
Example 49	0.1	0.62	Example 50	NT	2.32
Example 53	6.4	<20	Example 54	0.2	<20
Example 55	0.3	1.90	Example 57	0.8	0.48
Example 58	300	1.62	Example 59	0.4	1.33
Example 60	0.5	1.92	Example 61	4.3	NT

a : Inhibition of K-ras transformed cell growth

b : Inhibition of *In vitro* FPTase

NT : Not Tested

Table IV. (continued)

Compound	IC_{50}[a] (nM)	IC_{50}[b] (nM)	Compound	IC_{50}[a] (nM)	IC_{50}[b] (nM)
Example 63	2.3	1.30	Example 64	4.1	NT[c]
Example 66	0.1	0.94	Example 68	9.4	NT
Example 69	1.7	NT	Example 71	1.0	1.85
Example 72	2.0	3.70	Example 75	20.7	NT
Example 78	1.1	4.36	Example 79	2.0	5.33
Example 82	0.3	0.72	Example 83	16.0	NT
Example 85	4.8	NT	Example 87	0.1	0.72
Example 88	1.0	1.54	Example 89	0.2	1.45
Example 90	18.7	NT	Example 93	14.2	NT
Example 94	42.0	NT	Example 96	0.3	3.78
Example 97	1.4	3.30	Example 98	26.0	NT
Example 100	25.0	NT	Example 101	30.8	NT
Example 102	43.7	NT	Example 106	NT	0.65
Example 107	129.0	<10	Example 110	0.2	2.89
Example 111	0.3	2.73	Example 112	0.1	2.74
Example 113	0.3	NT	Example 114	0.2	3.66
Example 116	2.0	5.54	Example 117	52.0	<20
Example 118	13.0	<20	Example 119	19.0	<20
Example 120	NT	3.16	Example 121	NT	1.73

a : Inhibition of K-ras transformed cell growth

b : Inhibition of *In vitro* FPTase

NT : Not Tested

5

Table IV. (continued)

Compound	IC_{50}[a] (nM)	IC_{50}[b] (nM)	Compound	IC_{50}[a] (nM)	IC_{50}[b] (nM)
Example 122	NT[c]	2.18	Example 123	NT	1.42
Example 124	NT	4.59	Example 125	NT	3.53
Example 126	380.0	1.96	Example 127	220.0	0.83
Example 129	NT	3.83	Example 130	NT	2.00
Example 131	NT	2.41	Example 132	2260	0.12
Example 133	900	1.30	Example 135	380	1.13
Example 136	450	0.54	Example 138	540	0.22
Example 140	1010	1.85	Example 142	900	0.65
Example 143	750	1.27	Example 146	4150	2.11
Example 148	2800	0.08	Example 149	360	0.73
Example 150	560	0.73	Example 153	170	0.77
Example 154	190	0.40	Example 155	50	0.35
Example 159	NT	30.5	Example 160	3120	10.0
Example 163	1630	NT	Example 164	2310	NT
Example 165	1390	NT	Example 168	1230	NT
Example 169	2970	NT	Example 172	2110	NT
Example 175	1144	NT	Example 178	1750	NT
Example 182	22990	NT	Example 185	2430	NT
Example 186	NT	<10	Example 187	NT	8.8

a : Inhibition of K-ras transformed cell growth

b : Inhibition of *In vitro* FPTase

NT : Not Tested

Table IV. (continued)

Compound	IC_{50}[a] (nM)	IC_{50}[b] (nM)	Compound	IC_{50}[a] (nM)	IC50[b] (nM)
Example 189	NT[c]	1.66	Example 190	NT	2.50
Example 192	NT	2.25	Example 194	NT	3.52
Example 197	900	<10	Example 200	1850	NT
Example 201	2680	NT	Example 202	1850	NT
Example 203	NT	<10	Example 206	430	0.15
Example 207	160	NT	Example 208	190	1.63
Example 210	160	NT	Example 211	530	NT
Example 213	80	0.90	Example 214	14.0	0.37
Example 215	540	1.76	Example 217	360	1.61
Example 220	310	0.27	Example 222	220	<10
Example 223	180	<10	Example 224	530	0.18
Example 225	50	<10	Example 227	1330	<10
Example 229	1230	0.51	Example 230	890	<10
Example 232	1780	<10	Example 236	0.06	<10
Example 237	3490	<10	Example 240	1.74	<10
Example 242	3530	0.63	Example 243	1540	0.72
Example 244	940	0.40	Example 245	1330	0.31
Example 246	270	0.16	Example 247	330	0.12
Example 250	1320	0.73	Example 252	80	0.42

a : Inhibition of K-ras transformed cell growth

b : Inhibition of *In vitro* FPTase

NT : Not Tested

Table IV. (continued)

Compound	IC_{50}[a] (nM)	IC_{50}[b] (nM)	Compound	IC_{50}[a] (nM)	IC50[b] (nM)
Example 253	80	0.23	Example 254	2300	0.02
Example 255	440	0.35	Example 256	440	0.29
Example 258	880	<10	Example 260	880	0.66
Example 261	220	<10	Example 262	60	<10
Example 264	190	0.80	Example 266	1300	0.61
Example 267	3780	<10	Example 268	2460	<10
Example 270	1810	1.12	Example 271	NT[c]	<30
Example 273	NT	<30	Example 274	5300	<100
Example 276	2660	1.21	Example 277	2150	2.82
Example 279	100	<10	Example 280	40	0.81
Example 281	280	NT	Example 282	1060	<10
Example 283	30	<10	Example 284	10	0.32
Example 287	1940	<10	Example 288	1420	<10
Example 290	3390	<10	Example 291	2250	<10
Example 293	3400	<10	Example 295	1010	<10
Example 296	1390	<10	Example 299	2870	<10
Example 301	2970	<10	Example 302	440	1.42
Example 303	1190	1.51	Example 304	670	0.50
Example 305	860	<10	Example 307	490	<10

a : Inhibition of K-ras transformed cell growth

b : Inhibition of *In vitro* FPTase

NT : Not Tested

5

Table 1. (continued)

Compound	IC_{50}[a] (nM)	IC_{50}[b] (nM)	Compound	IC_{50}[a] (nM)	IC50[b] (nM)
Example 308	470	<10	Example 309	460	<10
Example 310	80	<10	Example 311	20	0.20
Example 313	590	<10	Example 315	20	0.38
Example 316	5.0	0.21	Example 317	8.4	0.24
Example 319	560	<10	Example 320	210	<10
Example 322	150	<10	Example 324	580	<10
Example 325	220	<10	Example 326	130	<10
Example 328	NT	4.74	Example 330	NT	0.39
Example 331	NT	0.69	Example 332	NT	0.20
Example 333	1.6	0.30	Example 341	NT	0.15
Example 342	NT	0.97	Example 343	NT	0.66
Example 344	NT	2.76	Example 345	NT	>10
Example 346	NT	0.71	Example 347	NT	1.84
Example 349	NT	2.37	Example 350	NT	2.11
Example 351	NT	1.07	Example 352	NT	6.76

a : Inhibition of K-ras transformed cell growth

b : Inhibition of *In vitro* FPTase

NT : Not Tested

From results of Table IV, the compound of formula (I) according to the present invention were identified as having a potent inhibitory activity against K-ras transformed cell growth and an ability to inhibit FPTase effectively.

Assay 3 : Inhibition of K-ras4B processing

NIH3T3 cells transfected with oncogenic human K-ras4B were plated in 6-well plate and cultured until the cell concentration reached at 10^5 per well. The cells were treated for 48 hours with either vehicle or the test compounds (0.1, 1, 10μ M). Cells were washed and lysed in 1 ml of lysis buffer (1× PBS(phosphate buffer saline), 1% Triton X-100, 1 mM phenylmethyl- sulfonyl fluoride, 25μg/ml leupeptin, 16μg/ml benzamidine HCl, 1 mg/ml Sigma-104 phosphate substrate) at 4℃ for 1 hour. Lysates were cleared (10,000 rpm, 4℃, 15 min), and equal amounts of protein were immunoprecipitated with the anti-ras antibody-agarose beads (OP01A, Oncogene Science) at 4℃ for 2 hours. The immunoprecipitated proteins were separated on a 15% SDS-PAGE, transferred to Hybond-ECL (Amersham Corp.), and immunoblotted using an anti-K-ras antibody (OP24, Oncogene Science). Antibody reactions were visualized using peroxidase-conjugated goat anti-mouse IgG and an enhanced chemiluminescence detection system (ECL, Amersham Corp.).

Posttranslational modifications have different effects on electro-phoretic mobility. Processed ras protein migrate slightly faster than their unprocessed counterparts. Therefore, the intensities of the bands corresponding to prenylated and nonprenylated K-ras proteins were compared to determine the inhibition of prenyl transfer to protein. The results of effective compounds presented in Table V reflects the ability to inhibit K-ras4B processing.

Table V. Inhibition of K-ras4B processing by compounds of this invention.

Compound	Inhibitory effect	Compound	Inhibitory effect
Example 214	610 nM[a]	Example 253	48%[b]
Example 311	47%[b]	Example 315	50%[b]
Example 328	55%[b]	Example 331	54%[b]
Example 332	360 nM[a]	Example 333	400 nM[a]

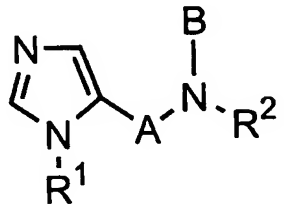
a : IC_{50}; b : inhibitory effect at 10uM

From the results of Table V, the compound of formula (I) according to the present invention were identified as having an ability to inhibit K-ras4B processing.

While the embodiments of the subject invention have been described and illustrated, it is obvious that various changes and modifications can be made therein without departing from the spirit of the present invention which should be limited only by the scope of the appended claims.

WHAT IS CLAIMED IS:

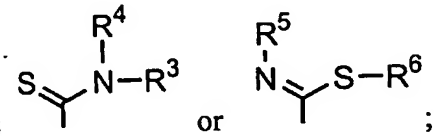
1. A compound of formula (I) or a pharmaceutically acceptable salt thereof:



(I)

wherein,

A is $-(CH_2)_n-$ or $-(CH_2)_n-C(=O)-$, n being an integer from 1 to 4;

B is  or ;

R^1 is C_{1-4} alkyl, or benzyl optionally having one or more ring substituents selected from the group consisting of cyano, nitro and methylenedioxy;

R^2 is C_{1-5} alkyl, C_{2-5} alkenyl; C_{5-7} cycloalkylmethyl; C_{1-3} alkylphenyl; a ring containing group selected from the group consisting of benzyl, α -methylbenzyl, naphthylmethyl, pyrrolymethyl, pyridylmethyl, indolylmethyl, and quinolylmethyl, each optionally having one or more ring substituents selected from the group consisting of C_{1-3} alkyl, halogen, C_{1-3} alkoxy, and trifluoromethyl;

R^3 is C_{1-10} alkyl; C_{2-5} alkenyl; C_{3-8} cycloalkyl; adamantyl; C_{1-5}-alkoxy-C_{1-5}-alkyl; mono- or di- C_{1-5}-alkylamino-C_{1-5}-alkyl; C_{1-5} alkoxylcarbonyl; phenyl-C_{1-5}-alkyl; tetrahydrofuranyl-C_{1-5}-alkyl; a nitrogen-containing heterocycle group selected from the group consisting of pyridyl, pyrimidyl, piperidyl, piperazyl, morphorinyl, and morphorinyl-C_{1-5}-alkyl, each heterocyclo being optionally substituted

with C_{1-3} alkyl or C_{1-3} alkoxy; an aromatic ring containing group selected from the group consisting of phenyl, naphthyl, and benzoyl, each optionally having one or more ring substituents selected from the group consisting of C_{1-5} alkyl, C_{1-5} alkoxy, C_{1-5} alkylthio, mono- or di-C_{1-5}-alkylamino, trifluoromethyl, benzyloxy, hydroxy, halogen, cyano, nitro, C_{1-5} alkoxycarbonyl, acetyl, and phenyl;

R^4 is hydrogen or C_{1-4} alkyl;

R^5 is phenyl optionally having one or more substituents selected from the group consisting of halogen, C_{1-5} alkyl, C_{1-5} alkoxy, and trifluoromethyl; benzyl; or pyridyl optionally substituted with hydroxy or methoxy; and

R^6 is C_{1-10} alkyl, C_{2-5} alkenyl, or benzyl with one or more optional ring substituents selected from the group consisting of C_{1-5} alkoxy, cyano and nitro.

2. The compound of claim 1, wherein

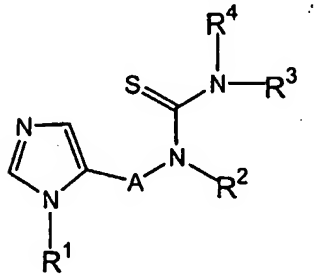
R^1 is benzyl optionally substituted with cyano, nitro or methylenedioxy;

R^2 is benzyl optionally substituted with halogen, C_{1-5} alkyl or trifluoromethyl;

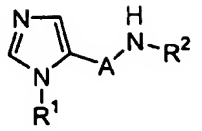
R^3 is C_{1-3} alkoxypyridyl; or phenyl optionally substituted with halogen, C_{1-5} alkyl, C_{1-5} alkoxy, trifluoromethyl, hydroxy, C_{1-5} alkylthio or C_{1-5} alkoxycarbonyl; and

R^6 is C_{1-10} alkyl.

3. A process for preparing a compound of formula (I-1) which comprises reacting a compound of formula (XXXII) with a compound of formula (XXXIII) or (XXXIV):



(I-1)



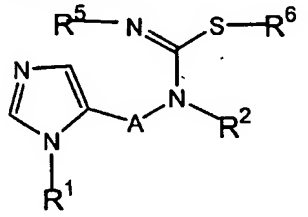
(XXXII)

(R^3)-N=C=S (XXXIII)

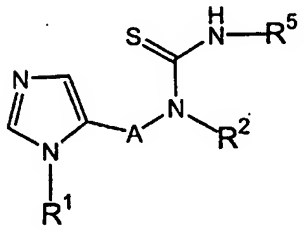
$(R^3)(R^4)$-N-C(=S)-Cl (XXXIV)

wherein A, R^1, R^2, R^3 and R^4 have the same meaning as defined in claim 1.

4. A process for preparing the compound of formula (I-2) which comprises reacting a compound of formula (If) with a compound of formula (XXXV):



(I-2)



(If)

R^6-X (XXXV)

wherein R^1, R^2, R^5, R^6 and A have the same meaning as defined in claim 1; and X is halogen.

5. A pharmaceutical composition for the inhibition of ras-transformed cell growth comprising a therapeutically effective amount of the compound or salt defined in claim 1 as an active ingredient together with a pharmaceutically acceptable carrier.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR00/00832

A. CLASSIFICATION OF SUBJECT MATTER

IPC7 C07D 413/12, A61K 31/41

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimun documentation searched (classification system followed by classification symbols)

C07D 413/12, A61K 31/41

Documentation searched other than minimun documentation to the extent that such documents are included in the fileds searched

Korean Patents and applications for inventions since 1975

Electronic data base consulted during the intertnational search (name of data base and, where practicable, search trerms used)

MEDLINE, NPS, PAJ, CA online

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
D, A	James GL et al.Polylysine and CVIM sequences of K-RasB dictate specificity of prenylation and confer resistance to benzodiazepine peptidomimetic in vitro' In:J. Biol. Chem., 1995 Mar, 270:11, 6221-6	5

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

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"A" document defining the general state of the art which is not considered to be of particular relevence

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
08 NOVEMBER 2000 (08.11.2000)	08 NOVEMBER 2000 (08.11.2000)

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Facsimile No. 82-42-472-7140	Telephone No. 82-42-481-5604

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